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VOLUME 92 NUMBER 2

Decadron®

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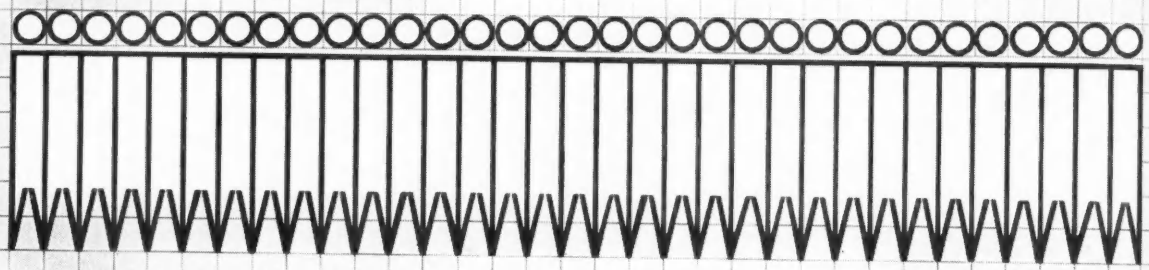
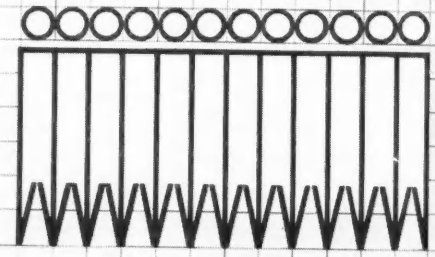
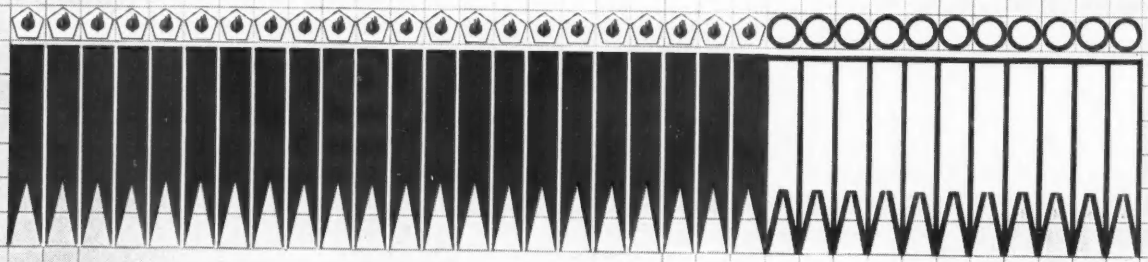
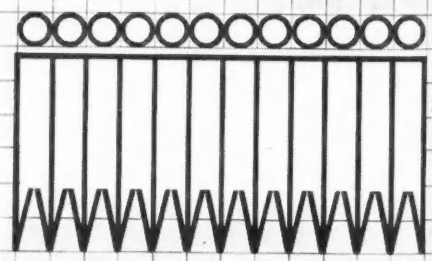


Of 45 arthritic patients
who were refractory
to other corticosteroids*





22 were successfully
treated with **Decadron**[1,2]



1. Boland, E. W., and Headley, N. E.: Paper read before the Am. Rheum. Assoc., San Francisco, Calif., June 21, 1958.
2. Bunim, J. J., et al.: Paper read before the Am. Rheum. Assoc., San Francisco, Calif., June 21, 1958.

*Cortisone, prednisone and prednisolone.

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California MEDICINE

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Volume 92 FEBRUARY 1960 Number 2

Newer Hormonal Preparations

ROBERTO F. ESCAMILLA, *M.D.*, San Francisco

• **A review of the present status of various hormonal substances is presented. The pituitary preparations include various growth hormones (human and beef), still used only experimentally, thyrotropic hormone, used mainly for testing thyroid function, corticotropin—widely used—and gonadotropic hormone.**

Thyroid, thyroxin and triiodothyronine preparations are considered, with USP thyroid still being most useful. Glucagon may be of some use in terminating hypoglycemia — tolbutamide is now used in many older diabetic persons. New adrenal cortical steroids are still appearing and show variation in effects; cortisone or hydrocortisone remain relatively inexpensive. Many combinations are available.

The newest addition to available male hormone preparations is fluoxymesterone which is anabolic in smaller dosage than the older forms.

Several new long acting preparations of androgens, estrogens and progesterone are available, and many ingenious combinations are presented.

IN PREPARING THIS PRESENTATION, it has become worth while to give a more than cursory glance to the carefully prepared advertising literature that pours across our desks, keeping in mind that if we consider only the newer preparations currently emphasized, we may not appreciate the entire picture of what is sound in endocrine therapy. Therefore this survey will be somewhat broader than indicated in the title.

Pituitary

It is known that the pituitary gland produces at least six different hormones.

The growth hormone (GH,STH), isolated and purified by Evans and Li in Berkeley, is now available only as prepared from human pituitaries. The supply therefore is extremely limited, but experimental trials have been promising. Attempts are being made to alter the beef growth hormone so that the molecule will approach the size of the human variety. If this preparation is biologically active in man it could provide a practical source of the hormone.

The thyrotropic hormone (TSH) is available as Thytropar® (Armour). Its principal use is in a test differentiating primary and secondary myxedema. After I^{131} uptake of the thyroid has been measured, TSH is administered in doses of 20 to 30 units daily for three days, and the uptake again measured. In normal persons the increase averages 20 per cent, in primary hypothyroidism the average is 7 per cent, while in secondary myxedema resulting from hypopituitarism the average increase of uptake is 32 per cent.

The gonadotropic hormones (follicle-stimulating hormone (FSH) and luteinizing or interstitial-cell-stimulating hormone (LH or ICSH)) are not available commercially in any satisfactory preparations. Gonadotropic effect can be obtained by using the chorionic gonadotropin from the placenta (APL,® Atuitrin S®). The same hormone extracted from the

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Submitted September 8, 1959.

serum of pregnant mares (Equinex®) has been disappointing clinically.

Lactogenic hormone. I know of no available commercial preparation.

Corticotropin (ACTH) is available in several preparations, and of course is widely used. The aqueous extract is relatively quick acting, while the gel is slower, lasting about 24 hours. Corticotropin zinc, however, lasts as long as 36 hours and in my experience has been a satisfactory preparation, although it occasionally causes some local soreness.

Posterior pituitary hormones. Neither the undifferentiated extract or the separated components vasopressin (Pitressin®) and oxytocin (Pitocin®) are new, but the exciting news is that both of the latter have recently been synthesized; synthetic oxytocin is now available commercially as Syntocinon®.

The melanophore-stimulating hormone (MSH), presumably from the pars intermedia, is now under investigation and may prove useful in such skin conditions as vitiligo.

Thyroid

Desiccated thyroid remains the most important hormonal agent in treatment of hypothyroidism, being generally satisfactory and the least expensive. If this proves unsatisfactory, perhaps Proloid® should be tried; it is a somewhat purified thyroglobulin that is occasionally better tolerated, without as many side effects as from thyroid. My impression is that milligram for milligram it is not quite as potent. Among the synthetic preparations, thyroxin is most commonly used as Synthroid,® a sodium levo-thyroxin of which 0.1 mg. is the approximate equivalent of 0.065 gm. (or 1 gr.) of USP thyroid. Incidentally, the dextro form of this substance seems to have little effect on the metabolism and therefore may have some special value (in investigations reported by Starr it apparently reduced the blood cholesterol).

Now that paper chromatography and other methods have disclosed that thyroxin is not the only active element in desiccated thyroid, we are hearing a great deal about the newly isolated substances—triiodothyronine, available as Cytomel® (levo-triiodothyronine) and Trionine® (dextro-levotriiodothyronine). These are slightly different in effect, but both act through their levo isomers, and reach the peak of effect rapidly, being excreted within 24 hours. In contrast a single dose of thyroxin may exert an effect for two to three weeks. Desiccated thyroid, of course, contains both. Occasionally, if quick action is desired, the newer forms may be more desirable, but thyroid USP is adequate in most instances. The push to promote triiodothyronine has even brought us a new diagnosis—"hypometabolism," which came initially from advertising promotion rather than from the scientific literature. Whether this exists as a separate entity is now being debated; I doubt that there is justification for the new term.

In dealing with overactivity of the thyroid, we should not forget iodine, which can be helpful, although the thiouracils now are being widely used. Propylthiouracil is the most popular, although in cases in which toxic reactions occur—blood cell changes or rash—the patient may tolerate methylthiouracil. Also used is methimazole (Tapazole®), which is effective in smaller dosage. Finally, there is a product available which incorporates iodine into the thiouracil molecule, Itrumil,® which also is helpful in some cases.

Parathyroids

For hypoparathyroidism one would naturally consider using parathyroid extract. It is available but unfortunately it evokes an antibody response rather quickly and is therefore effective for only a short period before the antihormone effect is apparent. For long-term therapy of hypoparathyroidism we must still rely on vitamin D, AT-10, calcium and dietary measures.

Pancreatic Islets

A new preparation causing hyperglycemia is glucagon, with an effect opposite to that of insulin. It can terminate hypoglycemia if administered intramuscularly, 1 to 2 mg. being the usual dose, with the effect apparent within 5 to 30 minutes. The usual accepted therapy, intravenous administration of glucose, may be more difficult if the patient is so unruly that restraint is necessary while the needle is being put into the vein.

For diabetes, the lente insulins are reported to be somewhat less allergenic than NPH but with similar action and are now available also as semilente and ultralente, so that we have available some variation in duration of action.

Although carbutamide has been abandoned in this country, tolbutamide (Orinase®) has stood the test of time fairly well as an orally effective agent, particularly for older patients. The manufacturer now reports several hundred thousand patients have taken Orinase® without serious side effects. An occasional clinical difficulty is that of patients' forgetting to take the second dose in a day. Orinase® is apparently so easy to take that it is more difficult to remember than insulin. If the patients respond well to Orinase® they frequently have a sense of well-being, almost euphoria, which is new to them.

A newer arrival in this very active field of investigation is chlorpropamide (Diabinese®), which has a somewhat longer action so that a single dose can be taken in the morning for the entire day. It is occasionally effective when Orinase® is not. Phenfor-

min® (DBI) is the latest addition to the group of oral hypoglycemic agents.

Adrenals

Both as a test and a remedy for pheochromocytoma—the adrenal medullary tumor which produces excesses of epinephrine and norepinephrine—we have Regitine.® This is especially useful during surgical extirpation of the tumor, and counteracts the discharge of an excess of these hormones into the bloodstream from manipulation.

Among the adrenocortical hormones for Addison's disease the older injectable extracts, both in aqueous and oily solutions, were valuable for many years; also DOCA (desoxycorticosterone acetate) has a good salt-retaining effect and is still a fairly good treatment in some patients with Addison's disease. There is also desoxycorticosterone trimethylacetate (Percorten® trimethylacetate), which has a prolonged action and can be given intramuscularly every four to six weeks in doses of 50 to 75 mg. Although cortisone has simplified the treatment of this condition, it is generally accepted that it is still best to combine a cortisone-like steroid with one of the salt retainers, such as DOCA, or the more recent fludrocortisone (Florinef®).

For comparison of potency, we can consider a 25 mg. tablet of cortisone to be equal to 20 mg. of hydrocortisone, which is thought to be closer to the true secretion of the adrenal cortex. Prednisone, which appeared next as Meticorten®, and prednisolone (Meticortelone®), both are approximately equally effective in doses of 5 mg. After these came triamcinolone (Aristocort® and Kenacort®), used in doses of 4 mg. These latter drugs, particularly, did not cause as much fluid retention. The next to appear was methyl prednisolone (Medrol®), effective in doses of 2 to 4 mg. And the latest at this time is dexamethasone (Decadron,® Deronil,® Gammacorten®), with dosage of 0.5 to 0.75 mg. Unfortunately, even though the amounts are small, the prices are high on the newer drugs; cortisone and hydrocortisone are still useful and are generally the least expensive. Fludrocortisone is also potent in small doses—0.1 to 0.3 mg.—but because of its salt-retaining effects is best used with cortisone for better control of Addison's disease. Also worth mentioning is hydrocortisone hemisuccinate (Solucortef®), which can be injected either intramuscularly or intravenously in an emergency and may be lifesaving.

The pharmaceutical industry has shown an impressive ingenuity in offering combinations of these steroids. Among skin ointments for instance, Metiderm® first appeared with prednisolone; later it was offered with Neomycin. I received a brochure recently announcing a product called Neo-Cort-Dome® which contains hydrocortisone plus Neomycin; and another, Cort-Tar-Quin,® contained hydrocortisone, plus tar, plus hydroxyquinolone; yet another, Histacort-E,® included hydrocortisone, vitamin A and an estrogen.

For arthritis there is also an abundance of preparations, each combination, of course, having a copyrighted name, which is understandable. One of the latest is Stenisone® which contains prednisone plus an anabolic agent and a gastric protector. Aristogesic® is an Aristocort® combination with salicylamide, aluminum hydroxide and vitamin C. Sterazolidin® contains prednisone, Butazolidin,® magnesium trisilicate and homatropine methylbromide (an anti-cholinergic), all in the same tablet. Varied combinations are also available as nose drops, eye drops and so forth.

Testes

Following the synthesis of testosterone, the first product commercially available was testosterone propionate in oil for intramuscular injection; this is still a good preparation and is relatively inexpensive. Next available was methyltestosterone, which was effective when taken orally although in larger dosage, and is somewhat more effective when used sublingually or bucally. Then followed the long-acting testosterones which could be injected every two to four weeks. Depo-Testosterone® (cyclopentylpropionate) was the first. Then Ciba made available testosterone phenylacetate, called Perandren® phenylacetate, as a suspension of macrocrystals. One of the more recent is Squibb's enanthate form, Delatestryl.® A new form for oral administration is fluoxymesterone, which is available as Halotestin,® Oratestryl® or Ultrandren.® This is five to ten times as effective as methyltestosterone by weight, and therefore is available in 2 mg. and 5 mg. tablets rather than the usual 10 mg. Unfortunately it is not that much cheaper; but it is a good anabolic agent, although not as potent in sexual stimulation, and is effective when swallowed.

Ovaries

Among the estrogens, estrone was first made available as Theelin® by Parke-Davis. Later came Schering's Progynon® (estradiol), also available in the dipropionate and benzoate forms. More recently, estradiol valerate has been brought out by Squibb as Delestrogen.® It is an effective long-acting preparation which may be injected at two to four-week intervals.

In most cases oral administration is satisfactory —Premarin,® a conjugated form, is usually effective at a dose of 1.25 mg. daily. However, the synthetics are cheaper, including stilbestrol 0.5 to 1 mg., or dienestrol 0.5 mg. Ethinyl estradiol is the most po-

tent by weight, the usual dose being .05 mg. daily. This is available as Estinyl® and as Eticylol.®

In this field too, there are numerous combinations, such as Premarin® with meprobamate and a host of others.

Among the progestins, progesterone usually must be injected, although it has some value when taken sublingually. A long-acting progesterone now available is Delalutin,® (hydroxyprogesterone caproate). Among the preparations for oral use, ethisterone (Pranone,® Lutocylol®) has been used for a number of years; it has been pointed out that the chemical formula for this preparation can be written so that it looks like one for ethinyl testosterone, and the confusion is compounded by the fact that ethisterone does have a slight masculinizing effect. Norlutin® (norethindrome), an effective oral preparation, has recently been released by Parke-Davis, and another recent addition is Enovid® which is a progesterone combined with an estrogen derivative. The vaginal route has been suggested for administration of progesterone, but I believe there is seldom need for this, as other routes are satisfactory.

Sex hormones in combination are many. There are estrogen-progesterone combinations available as Cyclogestrin® and Prometron.® Numerous estrogen-androgen combinations are available and since these are used rather frequently for osteoporosis it might be worth while to name a few. Lilly combines stilbestrol and methyltestosterone as Tylosterone®; these are also combined with reserpine under the name of Tylandrin.® Dienestrol and methyltestosterone are offered by White as Estan®; I use it fairly often because it is relatively inexpensive. Ayerst offers Premarin® with methyltestosterone. The male hormone is also combined with ethinyl estradiol—Femandrin® (Ciba) and Gynetone® (Schering)—and with estrone or estradiol in Theelandrol® (Parke-Davis), Combandrin® (Pfizer) and Dumone® (Squibb). Dela-Dumone® is an injectable long-acting estrogen-androgen combination of testosterone enanthate and estradiol valerate. Upjohn combines Halotestin® and estradiol as Halodrin® for oral administration; it may have some advantage in being slightly less virilizing in women, although it can cause enlargement of the clitoris.

As an example of adding extra items to a known effective combination in order to have a distinctive proprietary name, Ayerst combines Premarin® and methyltestosterone, then adds 400 mg. of vitamin C to make a preparation called Formatrix.®

For senility, a number of shotgun preparations are available. There have been some studies of sex hormone therapy which seem to justify use in the elderly—not only to help osteoporosis, but to improve senile changes in the skin and sometimes cause a general feeling of well-being. Accordingly, in Mediatric,® Ayerst includes a small dose of Premarin,® a small dose of methyltestosterone, and also vitamins, iron and desoxyephedrine—for a lift. One on which I was recently detailed is Eldec® of Parke-Davis, which contains Theelin® as an estrogen, plus some methyltestosterone, plus some pancreatin, plus other digestive ferments, plus vitamins and plus minerals!

DISCUSSION

DR. ALLAN HINMAN (chairman): I happen to be on the advertising committee of CALIFORNIA MEDICINE, which I think is the busiest committee of the state association. We meet once a week for two hours to ponder the claims made for new pharmaceuticals. We have a rather long list of rules that might be summed up as, "We will permit the truth to be stretched but not shattered." Sometimes even this line is hard to draw, because the men who write these ads are very adept. We spend most of our time on combinations.

We've received two questions for Dr. Escamilla: "What are the advantages, if any, of the new brominated form of desiccated thyroid?"

DR. ESCAMILLA: This is not particularly new. Thyrobrom® has been available for at least 20 years as I recall. It is said to relieve nervousness in the patient who otherwise would not receive the full benefit of desiccated thyroid, and is a combination that should not be used except in very special cases. Ordinarily, if side effects limited the necessary dose of thyroid I would try Proloid,® and if that is unsatisfactory try the triiodothyronines. The bromide combination, of course, carries the danger of bromism.

DR. HINMAN: Another question: Does the expression "more potent, milligram for milligram" signify any practical advantage? Why not simply use a larger dose of a less potent form?

DR. ESCAMILLA: This expression is heard frequently. The choice depends on whether the more potent form has the same effect and whether it presents other advantages. Among the adrenal steroids, for example, hydrocortisone in a 20 mg. dose and triansinolone 4 mg. have about equal effect in many ways, but the hydrocortisone causes more fluid retention, and therefore the more potent form has an advantage.

There is always hope, too, that the drug effective in smaller dosage will be cheaper for the patient, but it seldom works out that way. The pharmaceutical companies seem to figure that if 2 mg. of their product is as good as 10 mg. of another it should cost the same, or more, and we lose an advantage which I think should accrue to the patient.

384 Post Street, San Francisco 8.

Pheochromocytoma

A Report of 12 Cases

FRANK de M. HILL, *M.D.*, and DONALD R. SMITH, *M.D.*, San Francisco

• **In a series of 12 cases of pheochromocytoma, 11 patients were clinically cured by operation and one died of malignant tumor.**

It has been reported that of patients presenting with hypertension, 0.5 to possibly 2 per cent will be found to have pheochromocytoma. This small group of patients will have a good chance of cure of hypertension by surgical removal of the tumor.

Hypertension and manifestations of hypermetabolism are classically seen in pheochromocytoma, but these symptoms vary, and hypertension may be entirely absent.

Hypertension which is no longer dependent on pressor amines may result after prolonged circulation of pressor substances in the bloodstream. The quantity and proportion of the pressor amines in the circulation are largely responsible for the variable clinical picture.

The Regitine® test is an excellent screening test but is not absolutely specific for pheochromocytoma.

The histamine test should not be employed in patients whose blood pressure exceeds 160/110 mm. of mercury, lest it set off cerebrovascular accident.

A modification of the Garlock transdiaphragmatic incision that was used in the present series of cases affords unparalleled exposure and facility in the removal of pheochromocytoma.

THE OCCASIONAL REPORT concerning the clinical features of a particular case of a rare tumor of the endocrine system is likely to lack general interest if it has been established that tumors of the particular kind in question follow a uniform clinical pattern. Certainly pheochromocytoma masquerading as essential or "labile" hypertension, as diabetes mellitus, as thyrotoxicosis or occasionally as a psychoneurosis does not fall into this category. The series of 12 cases here presented is reported in the hope that a more precise clinical picture will eventually be formed.

Pheochromocytoma derives its name (*phaios*, dusky; *chroma*, color) from the dark brown color which most chromaffin tumors assume when treated with potassium dichromate. As a clinical entity, pheochromocytoma is comparatively new, the first case having been reported in 1886 by Fränkel, who observed bilateral adrenal medullary tumors at autopsy in a girl of 18 who died in coma. The first correct preoperative diagnosis and successful removal of a pheochromocytoma is credited to Pincoffs[7] in 1929. In the same year, Rabin determined the amount of epinephrine in a pheochromocytoma and, finding it to be in excess of that in the normal adrenal medulla, ascribed the clinical symptoms to this change.[13]

Pheochromocytoma is relatively rare—a total of approximately 325 cases reported to date. In patients in whom the presenting symptom was hypertension, the incidence was estimated by Smithwick to be 0.5 per cent.[9] Other investigators have thought the incidence in such cases may be 2 per cent or even higher. This constitutes a small, but potentially curable group of hypertensives and is in marked contrast to the balance of patients (except those with unilateral renal artery disease) for whom there remains only palliation. Three instances of pheochromocytoma have been reported in two members of a family, and Roth[8] reported bilateral tumors in three siblings. We include in this series two siblings who had this tumor and whose father had bilateral pheochromocytoma.

SYMPTOMS

In patients with pheochromocytoma the classical presenting feature is paroxysmal or sustained hypertension. Sweating, palpitations, anxiety, severe headache, flushing, nausea and vomiting are frequent symptoms. Other associated phenomena include paresthesias, thoracic or abdominal pain, cold, clammy or blanched extremities, as well as gradual impairment of vision, pronounced congestive failure or cerebrovascular accident which eventually develops unless the tumor is removed. The clinical complex of symptoms is extremely variable; many of the symptoms that are usually present, including hypertension, may be entirely lacking in some cases. A young tumor will generally give rise to less frequent periods of acute symptoms and more clinically dormant phases than an older tumor. After long periods and repeated attacks, the patient may acquire persistent rather than paroxysmal hypertension because of irreversible renal changes.[3] Not only do the duration and frequency of paroxysms influence the symptom complex, but also the probably constantly varying amounts and proportion of the vasospastic hormones play an important role.

From the Department of Surgery, Division of Urology, University of California School of Medicine, San Francisco 22.

Presented before the Section on Urology at the 88th Annual Session of the California Medical Association, San Francisco, February 22 to 25, 1959.

The frequency of attacks varies from ten or more per day to an isolated episode every few months. Most of the patients in the present series had paroxysms three or four times a week. Paroxysms usually lasted 5 to 10 minutes, occasionally longer, sometimes for only a few seconds. A variety of stimuli causing discharge of pressor amines from the tumor have been observed, among them changes in posture, pressure over the tumor, emotion, overindulgence in eating, shock, sneezing, singing and even voiding.

PATHOPHYSIOLOGY

Epinephrine alone was originally thought to be responsible for the symptoms of pheochromocytoma, this pressor substance being liberated from the adrenal tumor into the circulation. It was soon evident, however, that certain features of a typical attack were not explainable on the basis of the epinephrine effect alone. In 1949 Holton[4] discovered norepinephrine in normal adrenal medullary tissue, as well as in pheochromocytoma; and in the latter, concentration of norepinephrine could exceed that of epinephrine tenfold. Since then, the discovery and differentiation of pressor amines in the circulation have helped to explain the source and mechanism of an individual attack.

Epinephrine alone administered intravenously produces most of the manifestations of a typical paroxysm—abrupt rise in systolic blood pressure, anxiety, mydriasis, blanching of hands and feet, tachycardia, dyspnea and sweating, probably through sympathetic excitation. Norepinephrine in therapeutic doses has been shown to cause an increase in diastolic and systolic blood pressure and bradycardia but with few other subjective symptoms. The attempt at correlation of symptomatology with pressor analysis of the pheochromocytoma was more difficult until Goldenberg[2] and co-workers in 1950 demonstrated the difference in response to small and large doses of the two amines given intravenously to dogs. This study suggested that the tumor's pressor amine secretion could fluctuate in quantity and probably also in quality irrespective of the analysis of pressor content of the tumor, and consequently produce varying symptoms.

Patients with an intermittently discharging pheochromocytoma usually have paroxysmal hypertension, while others with a constant secretion of pressor amines have sustained hypertension. Goldenberg in 1950 found that intermittent or continuous discharge of pressor amines could be associated with persistent hypertension, implying that after prolonged circulation of pressor substances in the blood the ensuing hypertension may no longer depend on the circulating amines.

Symptoms of sustained hypermetabolism but paroxysmal hypertension may be explained on the assumption that a basal epinephrine secretion adequately meets the needs of hypermetabolism but is insufficient to produce the hypertension until epinephrine secretion increases suddenly.[6]

DIAGNOSIS

Pharmacological tests help greatly in the diagnosis of pheochromocytoma. Following the establishment of a patient's base-line blood pressure a cold pressor test is performed, followed by a histamine test. If the systolic and diastolic pressures rise roughly 60 mm. and 30 mm. of mercury, respectively, the result is "positive" provided the readings are in excess of that of the cold pressor test. This comparison will rule out the "hyper-reactor," as shown by Roth and Kvale.[5,8] We restrict the histamine test to patients whose blood pressure does not exceed 160/110 mm. of mercury and thereby reduce the incidence of catastrophes such as cerebrovascular accidents which can result from extreme pressor responses.

Regitine® has been used in most of the cases in this report. We have found it to be an easily administered and safe drug and well suited to a routine screening test. If pheochromocytoma is suspected and the blood pressure exceeds 170/110, Regitine® is the drug of choice for a screening test. The result of the test is "positive" if there is a decrease of more than 35 mm. of mercury in systolic and 25 mm. diastolic readings, both occurring within two minutes after intravenous injection.

The quantitative assay of pressor amines in the blood is the most direct and precise aid at present in diagnosis. The specimen of blood must be taken during or immediately following an acute episode if the results are to be significant. The normal values vary with the different laboratories but generally range from 3.5 to 5 micrograms of norepinephrine and about 0.5 micrograms of epinephrine per liter of blood as upper limits of normal.

During a normotensive phase, a rise in blood pressure may be brought about by the intravenous administration of 0.025 mg. or less of histamine base. If a blood specimen is drawn at the height of the blood pressure rise, levels of catechol amines of more than 20 micrograms per 100 cc. indicates the presence of a pheochromocytoma.

Urinary catechol amines are also of diagnostic significance. They will be found only in specimens taken during a period of active secretion by the pheochromocytoma. In the past these have been reported as total catechol amines assayed by a fluorometric technique. More recently, separate determination of the urinary epinephrine and norepinephrine has become available. Normal excretion should not exceed 50 and 200 micrograms per 100 cc., respectively, for these substances.[2,11,12]

An invaluable aid in the diagnosis of pheochromocytoma is intravenous pyelography. It should be carried out to supply one of the pieces of evidence which should be assembled before diagnosis is made. If the tumor is large enough, it will usually be seen as an ovoid soft tissue mass in the region of the adrenal gland and occasionally overlying a kidney. However, one must be careful not to misinterpret fluid in the stomach as a left suprarenal mass. The tumor will frequently displace the longitudinal calyceal axis of the kidney laterally and inferiorly. We believe that, excepting an obvious adrenal tumor mass seen on pyelography, the described change in axis of the calyces of a kidney, even to a slight degree, is the most suspicious sign of adjacent tumor mass. Calyceal distortion is rarely seen in pheochromocytoma and, barring primary renal lesions, would indicate invasion of renal parenchyma by malignant tumor.

If better delineation of perirenal structures is desired, we have used retroperitoneal oxygen insufflation and tomography with excellent result.[10] If such procedures or the pyelogram localize a suprarenal tumor, they become valuable aids to the surgeon in selection of an operative approach.

In the present series aortography has been employed on one occasion only (Case 7). In that case the procedure localized a very small tumor not seen in pyelographic or in oxygen studies. As a rule aortography is considered to be not without significant hazard in pheochromocytoma, for the added trauma may precipitate a fatal hypertensive attack.

SURGICAL ASPECTS

The recording of the blood pressure of the patient with pheochromocytoma at 1 or 2-minute intervals before and during all phases of anesthesia and operation is imperative and frequently lifesaving. In addition to the anesthetist, one member of a medical team of two persons records the blood pressure and the other controls the intravenous administration of fluids. We have used a blood pressure cuff in the past, but in our most recent case we resorted to a continuous arterial pressure-recording device, which necessitated brachial arteriotomy and catheterization. The removal of the pheochromocytoma in that case was uneventful. However, in the evening of the operation the patient complained of severe ischemic pain in the forearm, and the radial and ulnar pulses were absent. When an arteriogram revealed a complete block in the brachial artery just proximal to the bifurcation, the artery was again opened and thrombectomy performed. Following this the edema, numbness and duskiness of the hand and forearm gradually resolved. While arteriotomy is usually not considered a hazardous procedure, we feel that the intermittent blood pressure recording with a cuff is more than adequate and entails no risk whatsoever.

During the period between induction of anesthesia and the postoperative phase, the blood pressure is controlled by intravenous administration of Regitine® or Levophed® (L-norepinephrine) or 5 per cent dextrose and water, as needed. Characteristically, the blood pressure fluctuates throughout operation, rising perhaps with induction of anesthesia or the skin incision. A maximal rise usually occurs as the tumor is palpated and sporadic decreases then occur as the veins of the tumor are ligated. Pronounced hypotension is usually noted on removal of the tumor.

We favor the Garlock transdiaphragmatic approach for a pheochromocytoma that is demonstrated radiographically to be unilateral. Our modification of this incision is to make it between the ninth and tenth ribs with division of the costal cartilage. This affords unparalleled access and exposure for the surgeon and facilitates ligation of the veins from the tumor. Troublesome bleeding occasionally encountered from the vena cava is also more easily controlled. Also with this approach there is minimal palpation of the tumor mass during the dissection. This is an important consideration because, besides the likelihood of causing severe hypertension, palpation can easily lacerate the thin fibrous capsule of a pheochromocytoma and allow extrusion of the soft vascular tumor tissue into the retroperitoneal space. In light of the fact that some 10 per cent of pheochromocytomas are malignant, excision should be as meticulous as any procedure for the removal of a tumor known to be malignant.

For dealing with a pheochromocytoma that cannot be demonstrated by radiographic studies to lie in the suprarenal areas or with a tumor suspected of being bilateral, we would prefer an elongated paramedian abdominal incision extending from xiphoid process to symphysis pubis. This again offers maximal exposure for exploration of both adrenal areas as well as the abdominal cavity. Since the tumor may lie in any area where chromaffin tissue is found, a thorough abdominal exploration, including close inspection of the great vessels and the base of the small bowel mesentery, is indicated. Pheochromocytomas have been found in the urinary bladder, in the chest and in other areas, but these are rare.

REPORTS OF CASES

CASE 1. A 46-year old white male truck driver was admitted to the University of California Hospitals on January 24, 1944. In the preceding four years he had had "spells" consisting of dizziness, nervousness, palpitations, a slow, pounding pulse, headache and occasional nausea and vomiting. These episodes occurred about five times a day and lasted 8 to 10 minutes. The diagnosis at that time was acute anx-

iety state with hyperventilation syndrome and the patient was referred to the psychiatric clinic.

The patient was readmitted on January 15, 1947, after being observed in a typical attack in a physician's office. The patient had suddenly become anxious, his head and neck became cyanotic and his blood pressure rose from 150/90 to 250/110 mm. of mercury and then dropped to normal 3 minutes after the attack began.

No abnormalities were noted on physical examination. The blood pressure was 160/80 mm. of mercury and the pulse rate 64. The results of routine laboratory tests were within normal limits. A histamine test was positive for pheochromocytoma. A glucose tolerance test was positive for increased epinephrine production. An electrocardiogram was interpreted as showing left ventricular hypertrophy, and in intravenous pyelograms a large right suprarenal mass was seen pressing the right kidney downward and laterally.

On February 1, 1947, through an incision over the bed of the twelfth rib, a pheochromocytoma lying beneath the remains of a grossly normal right adrenal was excised. The tumor weighed 490 gm. and contained 200 ml. of bloody fluid within a large cyst.

The postoperative course was fairly smooth and the patient was having no symptoms when he was discharged on the 17th postoperative day. As of his last letter in November, 1958, the patient continued to feel well and had worked steadily since discharge.

CASE 2. A 25-year old white housewife who was admitted to the University of California Hospitals on March 11, 1948, had been in excellent health until two and a half years before when she had episodes of blurry vision lasting 10 or 15 minutes, occasionally accompanied by typical Jacksonian seizures beginning in the left hand and associated with syncope. She was told by a physician on one occasion that her blood pressure during an attack was 240. Shortly before admission she began to have frequent occipital headaches, tinnitus, dyspnea on exertion and palpitations. She had had about 12 such attacks.

At the time of the physical examination the patient was noted to be slender and nervous and apparently not in acute distress. The blood pressure was 186/130 mm. and the pulse rate 108. The skin was flushed and the patient was perspiring. A loud systolic murmur and precordial thrust were noted. Routine laboratory tests revealed no abnormalities. An electrocardiogram was interpreted as showing left ventricular hypertrophy and sinus tachycardia.

A diagnosis of essential hypertension was made and a first stage left thoracolumbar sympathectomy was done March 17, 1948. On April 8, 1948, during the second stage right sympathectomy, a pheochromocytoma about 4 cm. in diameter lying just beneath a normal appearing right adrenal was discovered and excised. Symptoms did not recur in ten years of observation.

CASE 3. A 35-year-old white housewife, first admitted to the University of California Hospitals on May 15, 1952, said that she had had hypertension for three years. It was discovered first at the time of her first pregnancy. Later the patient experienced excessive perspiration, insomnia, nervousness and irritability, which had begun during her second pregnancy the following year. She also became aware of thirst, polyphagia, frequency of urination and moderate intolerance of heat. Previous to admission to hospital, a diagnosis of hyperthroidism had been made (basal metabolic rate of plus 72), and the patient had been given propylthiouracil under her physician's care, but her condition did not improve.

On physical examination it was noted that the patient was pale and obese. She perspired profusely and had cold clammy skin. The blood pressure was 130/90 mm. of mercury and the pulse rate was 110.

Results of routine laboratory tests were within normal limits. Intravenous pyelograms showed possible enlargement of the left adrenal gland. Results of cold pressor, benzodioxane and mecholyl tests were negative for pheochromocytoma. No abnormality was noted in a retroperitoneal oxygen study. Following mecholyl injection, the patient had crushing substernal pain; later, electrocardiographic changes suggested myocardial infarction. The patient then left the hospital against medical advice.

She was readmitted July 15, 1953, with progressive and severe symptoms of sweating, headache and impairment of vision of the right eye of one week's duration. A Regitine® test at this time was positive for pheochromocytoma. Intravenous pyelograms and retroperitoneal oxygen studies revealed a 7 cm. mass overlying the left kidney and displacing its upper pole laterally.

While awaiting operation, the patient noted beginning impairment of vision of her left eye. Intramuscular administration of 5 mg. of Regitine® every 6 hours was started to control hypertension.

On August 13, 1953, through a left Garlock transdiaphragmatic incision in the 9-10 interspace a well-encapsulated pheochromocytoma overlying the anterior aspect of the renal pedicle was removed. The tumor weighed 67 gm. and was 6.5 cm. in diameter. As the adrenal gland appeared to be normal and entirely separate from the tumor, it was not removed.

It was necessary to give Levophed® intravenously only during the first postoperative day and the patient was discharged on the ninth postoperative day.

When last examined in October, 1958, she had no symptoms and the blood pressure was 110/70 mm.

CASE 4. A 43-year-old white male pharmacist who was admitted to St. Luke's Hospital, San Francisco, on April 2, 1954, had had intermittent and severe attacks of nervousness, sweating, palpitations, upper abdominal discomfort and flushing of the face over a period of two years. The attacks lasted 10 to 20 minutes and occurred at about weekly intervals.

On physical examination this patient was observed to be nervous and hyperactive. The blood pressure was 160/110 mm. of mercury and the pulse rate 112. The facial skin was flushed, while that over the knees and elbows was decidedly cyanotic in blotchy areas. An active precordial heave was present.

On the second hospital day the blood pressure was 235/135 mm., then fell to 160/105 mm. within 10 minutes. During this hypertensive phase the patient was anxious and perspired profusely.

Abnormalities noted in laboratory tests included 4 plus proteinuria, leukocytes numbering 20,000 per cu. mm. A basal metabolic rate of +47, blood sugar content (fasting) 137 mg. per 100 cc. and nonprotein nitrogen of 65 mg. per 100 cc. The Regitine® test was positive for pheochromocytoma. A retroperitoneal oxygen study revealed a large tumor mass overlying the superior pole of the right kidney (Figure 1). The left adrenal gland was believed to be of normal size, although visualization was hampered by dilated loops of bowel.

On April 6, through a right Garlock transdiaphragmatic approach, a 200 gm. ovoid tumor measuring 10 x 8 x 4 cm. and enclosed by a thin ragged capsule was removed. The pathologist reported the tumor to be a malignant pheochromocytoma, with tumor cells invading the adrenal cortex.

It was necessary to maintain the patient's blood pressure with Levophed® until the fourth postoperative day when episodes of pronounced hypertension developed (blood pressure 240/170 mm. of mercury) with sweating, pallor, anxiety and increasing abdominal distention. X-ray examination with oxygen insufflation was repeated on April 16, and another large ovoid tumor mass was seen overlying the upper pole of the left kidney. This tumor had previously been erroneously thought to be a loop of bowel. The patient's family refused further operation, and death due to congestive heart failure followed within a week.

At autopsy a pheochromocytoma of about the same size as the one found on the right side, was observed above the kidney on the left. Hepatic metastatic lesions presumably secondary to the malignant right pheochromocytoma were also discovered.

CASE 5. A 71-year-old white woman entered St. Luke's Hospital, San Francisco, on March 5, 1955. She had had increasing attacks of nervousness, weakness, sweating, flushing, thirst and a ten-year history of poorly controlled diabetes mellitus and hypertension.

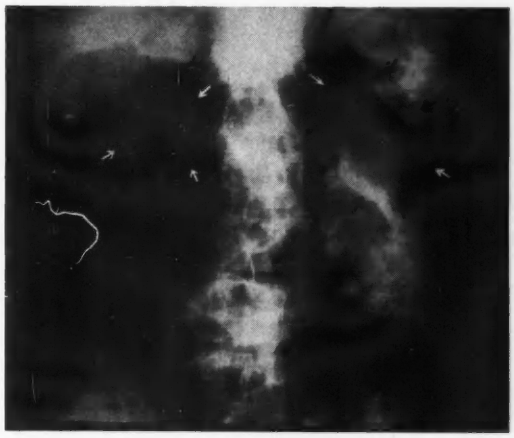

Figure 1 (Case 4)—Retroperitoneal oxygen study showing large bilateral pheochromocytomas. The left tumor was at first mistaken for a segment of dilated bowel.

Upon physical examination she was observed to be thin, prostrated and sweating profusely. The blood pressure was 210/110 mm. of mercury and the pulse rate 120. Except for evidence of cardiac enlargement no other abnormalities were noted. The blood sugar (fasting) was 296 mg. per 100 cc. and results of Regitine® and benzodioxan tests were positive. Intravenous pyelograms and retroperitoneal oxygen studies showed a mass 7 cm. in diameter overlying the superior pole of the left kidney.

On March 24, 1955, a 45 gm. pheochromocytoma was removed through a Garlock transdiaphragmatic incision between the ninth and tenth ribs. It was necessary to give Levophed® by slow infusion until the third postoperative day, and thereafter the course was uneventful. The patient was discharged from the hospital on the 21st postoperative day, with no symptoms. When she was examined thereafter no evidence of recurrence of the previous symptoms or glycosuria were noted and the blood pressure was within normal limits.

CASE 6. A 17-year-old white girl was admitted to the University of California Hospitals on July 6, 1955, with a history of intermittent attacks one to nine times a day consisting of headache, palpitations, nausea, vomiting, a sensation of numbness and paresthesia in both lower extremities, and sweating. These episodes lasted 3 to 10 minutes.

Her father had died at age 57 of a "stroke" and at autopsy was found to have bilateral pheochromocytomas. Her brother (see following case) also was later found to have a pheochromocytoma.

No abnormalities were noted upon physical examination. The blood pressure at the start of the examination was 160/90 mm. of mercury but rose shortly to 225/130 mm., and the rise was accompanied by substernal pain and sweating.

Results of laboratory studies were within normal limits. An electrocardiogram tracing was abnormal but nonspecific. The catechol assay of a 24-hour urine collection was 1,000 micrograms.

On July 13, 1955, a 250-gram pheochromocytoma was removed from the left adrenal area through a left Garlock transdiaphragmatic incision between the ninth and tenth ribs. The postoperative course was uneventful and vasopressors were not required.

A year and a half after the patient was discharged from the hospital, transient episodes of weakness, occasional headache and light-headedness, lasting 2 to 3 minutes, developed. Further studies were done but no evidence of another pheochromocytoma was found.

CASE 7. A 20-year-old white man, a laboratory technician, was admitted to the University of California Hospitals on July 9, 1955, at the prompting of his sister (see Case 6) because of a three-year history of recurrent attacks of palpitations, blanching of face and hands, tremor, numbness and tingling of the lower extremities and sweating. The attacks occurred 10 to 15 times a week and were of 5 to 20 minutes' duration. His sister had just been operated on for removal of pheochromocytoma at this hospital and his father at age 57 had died as the result of a cerebral vascular accident as a complication to bilateral pheochromocytomas discovered at autopsy.

On physical examination he appeared to be healthy and in no acute distress. The blood pressure was 135/80 mm. of mercury and the pulse rate 80. A grade II apical blowing systolic murmur was the only abnormality noted. Results of routine laboratory tests were within normal limits and no abnormalities were observed in pyelograms or in a retroperitoneal oxygen study. The results of a histamine test, glucose tolerance test and urinary catechols on two occasions were equivocal. The patient was discharged without a diagnosis of pheochromocytoma having been made.

He was readmitted on December 2, 1957, with complaint of more severe symptoms and more frequent attacks. A histamine test was strongly positive for pheochromocytoma; the blood pressure rose to 230/130 mm. of mercury from 120/80. Again intravenous pyelograms and retroperitoneal oxygen studies showed no abnormalities but an aortogram revealed a small tumor in the region of the right adrenal gland. On December 19, 1957, a 3 x 1.5 x 1.5 cm. pheochromocytoma was removed from the right suprarenal area through a right Garlock transdiaphragmatic incision between the ninth and tenth ribs. The patient made an excellent recovery and vasopressors were not given postoperatively. When last examined, in November, 1958, he was asymptomatic. The blood pressure was 120/85 mm.

CASE 8.* A 55-year-old white housewife was admitted to the University of California Hospitals on March 10, 1956, because of severe headaches, warm flushes and "choking sensations" during the preceding six months. These episodes occurred daily, usually lasting 5 minutes, and were precipitated when she lay on her left side. She had undergone total left and partial right adrenalectomy previously for Cushing's syndrome. At that time severe diabetes, virilization, with elevated 17 ketosteroids and 17 hydroxycorticoids had been noted and the diagnosis of Achard-Tiers syndrome had been made.

On physical examination the patient appeared to be healthy and to have no residual of Cushing's syndrome. The blood pressure was 165/85 mm. of mercury and the pulse rate was 88. There were no remarkable physical findings.

No abnormalities were seen in retroperitoneal oxygen studies. The basal metabolism rate and an electrocardiogram were within normal limits.

Shortly after admission the patient had an attack of hypertension, with blood pressure at 240/180 mm. of mercury for 10 minutes. A subsequent Regitine® test was positive for pheochromocytoma and urinary catechols were 1,100 micrograms in a 24-hour urine collection.

On March 27, 1956, the patient underwent operation, and through an upper transverse abdominal incision a pheochromocytoma 5 cm. in diameter that lay amidst the remnants of the right adrenal gland and was intimately adherent to the vena cava was removed. The patient made an uneventful recovery. Vasopressors were given until the fourth postoperative day. The patient was maintained on complete adrenal cortical replacement therapy, and when examined 20 months after the operation was having no symptoms. The blood pressure was 110/80 mm.

CASE 9.† A 59-year-old white male school teacher was admitted to the University of California Hospitals on June 17, 1956. For a year he had had paroxysmal bouts of palpitations, headaches, spots before his eyes, substernal ache, dizziness, weakness and tremor. The attacks varied in intensity, lasted 1 to 30 minutes and occurred at least once daily.

On physical examination the patient was observed to be thin. The blood pressure was 120/70 mm. of mercury and the pulse rate was 72. During rectal examination a typical attack suddenly developed with

*Courtesy of Doctors Peter Forsham and Maurice Galante.
†Courtesy of Dr. Frank Hinman, Jr.

a rise in blood pressure to 260/150 mm. This episode lasted 20 minutes.

A hemogram, urinalysis, fasting blood sugar and protein bound iodine were within normal limits. A urinary catechols assay revealed a borderline elevation of 160 micrograms in 24 hours. Histamine and Regitine® tests were positive for pheochromocytoma.

Tomograms of the adrenal glands suggested a tumor mass in the right adrenal area. In a retroperitoneal oxygen study an ovoid tumor 3 cm. in diameter was seen lying adjacent to the right adrenal.

On June 26, 1956, a right Garlock transdiaphragmatic incision was made between the ninth and tenth ribs and a pheochromocytoma 3 cm. in diameter lying posterior and medial to the adrenal gland was excised together with the right adrenal. The specimen weighed 19 gm.

The patient was dismissed from the hospital asymptomatic and with a blood pressure of 110/70 mm. of mercury on the tenth postoperative day.

Two years later he was readmitted to this hospital for transurethral prostatectomy. The blood pressure at that time was 120/80 mm. of mercury. The course of his stay in hospital was entirely uneventful.

CASE 10.‡ A 35-year-old white housewife admitted to the University of California Hospitals on March 30, 1957, complained of paroxysmal attacks of epigastric pain, palpitations, sweating and headaches occurring at very irregular intervals during the preceding two years and lasting 5 to 20 minutes. The physician who referred her had noted a labile blood pressure varying from 140/95 to 190/110 mm. of mercury during one visit.

The patient was an anxious, hyperreactive, well developed woman. The blood pressure was 125/90 mm. of mercury and the pulse rate 100. Upon cardiac examination, a forceful ventricular heave, cardiac enlargement and a systolic apical murmur were noted. An electrocardiogram revealed anterior myocardial ischemia. A hemogram and results of urinalysis were within normal limits. Results of histamine and Regitine® tests were positive for pheochromocytoma and the excretion of urinary catechols was reported to be 1,000 micrograms in 24 hours. Intravenous pyelograms and retroperitoneal oxygen studies revealed slight downward and lateral displacement of the upper pole of the kidney with a tumor mass 10 cm. in diameter lying just anterior to the kidney. On April 9, 1957, the patient was taken to the operating room, but immediately after she was transferred to the operating table, it became apparent that she had had incomplete right hemiparesis. The operation was postponed for ten days, the hemiparesis having almost disappeared by then. Through an extra-pleural eleventh rib approach a pheochromocytoma about 10 cm. in diameter was removed. Vasopressors were used until the third postoperative day. The patient was dismissed from the hospital asymptomatic on the 16th postoperative day. The blood pressure was then 110/70 mm. of mercury, and urinary catechol content was normal. She received physiotherapy for slight residual of the right hemiparesis.

‡Courtesy of Dr. Frank Hinman, Jr.

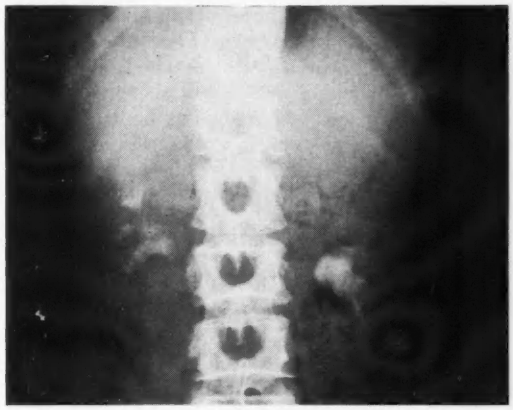

Figure 2 (Case 11)—Pyelogram demonstrating downward and lateral displacement of left kidney from a suprarenal mass.

CASE 11. A 53-year-old white saleswoman was admitted to the University of California Hospitals on June 15, 1957. She had had recurrent attacks of dizziness, weakness, palpitations, sweating, and headaches with occasional nausea and vomiting in the preceding four months. She said she had been "nervous" all of her life and had been told she was hypertensive five years before. The attacks occurred two to three times a day and lasted 10 to 30 minutes.

The patient was thin and anxious. The blood pressure was 160/85 mm. of mercury and the pulse rate 100. There was evidence of cardiomegaly and a Grade II systolic murmur was heard over the precordium. The results of urinalysis and of a hemogram were within normal limits. Significant findings included a Regitine® test positive for pheochromocytoma. The content of catechols in a 24-hour specimen of urine was 500 micrograms. During intravenous pyelograms the patient's blood pressure soared suddenly to 250/170 mm. and she had a typical attack. The pyelograms showed a suprarenal mass 10 cm. diameter displacing the left kidney downward (Figure 2). On June 28, 1957, through a left Garlock transdiaphragmatic incision, a large pheochromocytoma was removed. It was necessary to give the patient 400 mg. of Regitine® intravenously during a two-hour period in the operating room before the blood pressure descended to a level permitting induction of anesthesia. Levophed® drip was required

for only two hours postoperatively, and the postoperative course was benign. Four months after operation labile hypertension was noted, with blood pressure as high as 190/100 mm., but the urinary catechol assay was within normal limits. No evidence of another pheochromocytoma was discovered and the patient remained essentially asymptomatic.

CASE 12. A 17-year-old white single female was admitted to the University of California Hospitals on December 21, 1958. Four months previously, sweating, dizziness and nausea had occurred when she was singing in church. She also noted substernal pain, aggravated by exercise or deep breathing, as well as polydipsia and severe frontal headaches and night sweats. These attacks usually persisted for 1 to 3 minutes. This condition had been diagnosed as diabetes by a physician six weeks before her admission to the hospital, and she had been found to have Kimmelstiel-Wilson retinopathy and an abnormal glucose tolerance curve.

The patient was normal-looking and apparently in no acute distress, with a blood pressure of 150/110 mm. and a pulse rate of 80. The skin was generally moist. On examination of the eyegrounds, flame shaped hemorrhages, exudates and papilledema of the left fundus were noted. Cardiac examination revealed a precordial thrust and a Grade I systolic blowing murmur at the apex.

Leukocytes numbered 15,000 per cu. mm. of blood, 80 per cent polymorphonuclear cells. The sedimentation rate was 22 mm. in one hour. The basal metabolism rate was plus 52. A Regitine® test was strongly positive for pheochromocytoma. The plasma norepinephrine was elevated to 16 micrograms/liter and the plasma epinephrine to .58 micrograms/liter. The only abnormality observed in intravenous pyelograms was a slight axis deviation on the right, but retroperitoneal oxygen studies revealed a mass measuring 6 x 5 x 4 cm. overlying the right kidney in the adrenal area (Figure 3).

On December 30, 1958, a pheochromocytoma intimately adherent to the right adrenal was removed through a right Garlock transdiaphragmatic incision. The tumor weighed 30 gm. It was not necessary to give vasopressors postoperatively, and the patient's blood pressure stabilized at 170/100 mm. of mercury. Results of histamine and Regitine® tests and urinary catechol assay after operation did not suggest the presence of another pheochromocytoma.

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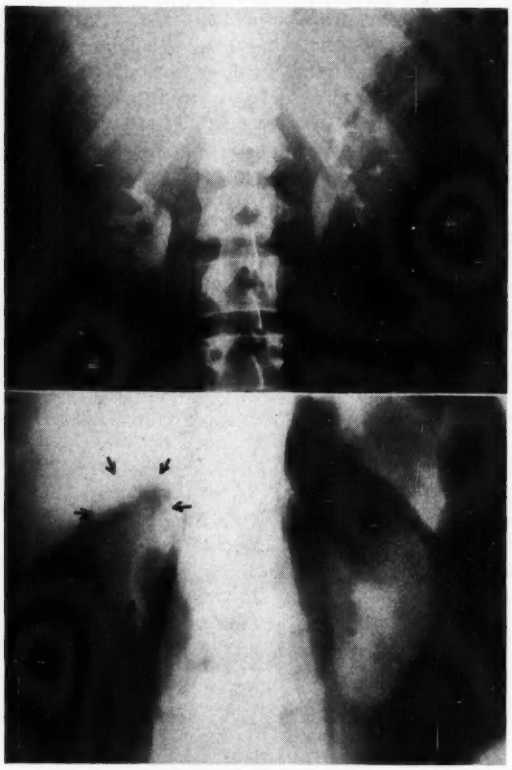

Figure 3 (Case 12)—*Above:* Pyelogram revealing abnormal vertical calyceal axis of right kidney and normal oblique axis on left. *Lower:* Retroperitoneal oxygen study showing right pheochromocytoma.

REFERENCES

1. Dybkaer, R., and Gjol, N.: Pheochromocytoma, some clinical symptoms and their patho-physiology, Acta Endocrinol., 26:450, 1957.

2. Goldenberg, M., Serlin, L., Edwards, R., and Rapport, M. M.: Chemical screening methods for diagnosis of pheochromocytoma; nor-epinephrine and epinephrine in human urine, Am. J. Med., 16:310, 1954.

3. Green, D. M.: Pheochromocytoma and chronic hypertension, J.A.M.A., 121:1260, 1946.

4. Holton, P.: Noradrenaline in adrenal medullary tumors, Nature, 163:217, 1949.

5. Kvale, W. F., Roth, G. M., Manger, W. M., and Priestley, J. T.: Present-day diagnosis and treatment of pheochromocytoma, J.A.M.A., 164:855, 1957.

6. Millar, R. A.: Pharmacology and pheochromocytoma, Brit. J. Anaesth., 29:50, 1957.

7. Pincoffs, M. C.: A case of paroxysmal hypertension associated with suprarenal tumor, Tr. A. Am. Physicians, 44: 295, 1929.

8. Roth, G. M., and Kvale, W. F.: A tentative test for pheochromocytoma, Am. J. M. Sc., 210:653, 1945.

9. Smithwick, R. H., Greer, W. E. R., Robertson, C. W., and Wilkins, R. W.: Pheochromocytoma, N.E.J.M., 242:252, 1950.

10. Steinbach, H. L., and Smith, D. R.: Extraperitoneal pneumography in diagnosis of retroperitoneal tumors, Arch. Surg., 70:161, 1955.

11. Von Euler, U. S., Hellner, S., and Purkhold, A.: Excretion of noradrenaline in urine in hypertension, Scandinav. J. Clin. & Lab. Invest., 6:54, 1954.

12. Von Euler, U. S.: Increased urinary excretion of noradrenaline and adrenalin in cases of pheochromocytoma, Ann. Surg., 134:929, 1951.

13. Watkins, D. B.: Pheochromocytoma: a review of the literature, J. Chron. Dis., 6:510, 1957.

Vomiting as a Symptom of Serious Disease In Infants and Children

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• **Vomiting or its lesser stages—anorexia, nausea—is a prime symptom of the most serious surgically curable diseases of childhood.**

In the newborn, when vomitus is green, abdomen scaphoid, and erect roentgen view shows air-fluid levels in stomach and duodenum with gas beyond, partial duodenal obstruction is present and midgut volvulus with malrotation is likely enough to justify immediate exploration.

In infancy, vomiting is a clear sign of intussusception when associated with intermittent colicky pain, palpable mass and "currant-jelly" feces. These symptoms are not always present, and if there is blood in the feces, barium enema study must follow. In further doubt, exploration may be justified.

In childhood, a common early symptom of appendicitis is vomiting accompanied by pain without any complete remission. Constipation is frequent but diarrhea may occur and contribute to an impression of gastroenteritis. Complete and repeated physical examination, with a history of the above symptoms, should lead to correct diagnosis.

STEADY ADVANCES in abdominal surgery are an outstanding feature of pediatric progress in the past decade. Digby Leigh and Katherine Belton of the Los Angeles Children's Hospital pioneered in pediatric anesthesia with the circle filter and the nonbreathing valve for infants, thereby eliminating dead space and making anesthesia safer. Endotracheal intubation was a further step in delivering more oxygen and less anesthetic, and the relaxant drugs contributed further to this end, besides producing better relaxation of the abdominal muscles. Hypothermia has been used to advantage in the desperately ill, febrile child with intestinal obstruction or peritonitis.[1] These skills have been widely disseminated by such teaching centers as the Los Angeles Children's Hospital.

Equally important progress has been made in preoperative and postoperative care of children. The fluid requirements of infants have been found to be much smaller than previously thought;[2] and infants' intolerance of salt overload is better understood. Accordingly, maintenance fluid and electrolytes are administered in smaller quantities and replacement fluid is both multi-ionic and hypotonic in character. With the use of antibiotics and isolettes, postoperative respiratory complications have been decreased. Typical of progress in special conditions is steroid support in certain metabolic disorders such as the adrenogenital syndrome.

All these improvements increase the value of surgical intervention in certain acute diseases of childhood; but they are of no value to the patient unless the diagnosis is suspected and steps are taken to verify it. Maintaining just the right degree of informed suspicion is not easy when every vomiting newborn must be examined and innumerable telephone calls about "bellyaches" answered. How is a clinician to know the case that requires operation?

The single symptom, probably most common throughout infancy and childhood, which can portend a serious or even fatal outcome is vomiting. It is well to note that anorexia and nausea are lesser degrees of the same symptom. Many causes of vomiting are obvious, but in each phase of childhood there is a lethal lesion which may cause vomiting as a presenting symptom and the diagnosis of which can easily be missed. These lesions are: in the newborn, midgut volvulus with malrotation; in infancy, intussusception; in childhood, appendicitis.

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Midgut Volvulus with Malrotation

Vomiting is common in the neonatal period, but green vomitus is not. Vomiting is characteristic also of tracheoesophageal fistula, but in that condition there is constant salivation, and feeding causes regurgitation associated with periods of cyanosis. Atresia or stenosis elsewhere in the gastrointestinal tract is distinguished by some degree of abdominal distention in addition to the vomiting.

In midgut volvulus with malrotation, the abdomen is scaphoid and the vomiting is intermittent, but the vomitus is almost invariably green. Meconium feces may be passed. Bloody feces, associated with a decrease in hemoglobin content, signifies vascular damage. The symptoms may be indistinguishable from those of duodenal obstruction but there is an important difference between these lesions, for midgut volvulus unless treated promptly may result in fatal gangrene of the small intestine; early operation is curative.

The most important single diagnostic aid in a patient with such symptoms is roentgen study. A view of the abdomen, with the patient erect, that

shows a "double bubble" (air-fluid levels in the stomach and duodenum), with a small amount of gas beyond, is diagnostic of partial duodenal obstruction, for which early operation is indicated. An upper gastrointestinal view is not needed. Barium enema study may give confirmatory evidence of the malrotation accompanying volvulus but may easily be omitted.

Intussusception

Vomiting in an infant is a clear symptom of intussusception when associated with intermittent colicky pain, a palpable mass and "currant-jelly" stool.[3] However, there is a variant of this disease in which the vomiting (in a previously healthy infant) is accompanied by cramping abdominal pain and bloody feces; this may be mistaken for gastroenteritis, especially as the symptoms are described by telephone. In intussusception, blood in the stool indicates some degree of vascular damage. Unless this diagnosis can be ruled out, an infant with these symptoms should have a barium enema study. When the lesion is ileocolic, the typical roentgen findings are diagnostic. Ileoileal intussusception is not ruled out by negative roentgen findings. Also, it should be remembered that there are two degrees of obstruction in intussusception—the "loose" and the "tight." "Loose" intussusception may be present for several days without vascular impairment, whereas gangrene may occur within hours after onset in the "tight" variety. Present practice at the Children's Hospital is to explore when in doubt and correct the intussusception. An initiating mechanism, such as a Meckel's diverticulum or polyp, is present in ten per cent of cases and must be excised.

Hydrostatic gravimetric barium enema reduction, with careful observation, is being advocated at some centers abroad and by Ravitch of Baltimore. The results of this therapy are being carefully followed but as yet this method is not in general use. Delay in the diagnosis of this lesion results in increased morbidity and mortality when resection of damaged bowel is required.[3]

Appendicitis

Although, volumes have been written about appendicitis, it behooves physicians to review the disease as it usually appears in the child from time to time. Here, too, vomiting is usually the initial symptom, accompanied by abdominal pain. If the pain has been continuous,[4] with exacerbations but without ever subsiding completely, appendicitis should be suspected at once. Again it may be stressed that anorexia and nausea are of the same nature as vomiting and equally significant. Athough bowel habit is altered in most patients with appendicitis, and most frequently toward constipation, an appreciable number have symptoms of vomiting, abdominal pain and diarrhea indistinguishable from those of gastroenteritis.[5] The following is a case in point.

A 12-year-old girl had abdominal pain, cramping in nature, followed by vomiting and diarrhea. She was examined at two clinics and once hospitalized in the course of a week, the diagnosis of gastroenteritis being considered on both occasions.

After her admission later to the Los Angeles Children's Hospital, a roentgen film of the abdomen showed advanced meteorism with dilated loops of small and large bowel. On physical examination the pelvis was tender and indurated, the abdomen distended but silent and not tender. The patient was treated preoperatively for 12 hours with intubation, fluids and antibiotics. A perforated pelvic appendix was then removed and enterotomy performed for decompression. Recovery was fairly rapid.

The history is still the most important factor in the diagnosis of appendicitis; combined with careful physical examination, repeated frequently[6] in equivocal cases, it leads to accurate diagnosis in the great majority. Laboratory tests are of course necessary although rarely diagnostic except when pus is found in the urine. In a child with appendicitis there is almost always some degree of nausea. Nausea accompanied by persistent pain or persistent localized tenderness, with or without rigidity, should arouse suspicion of appendicitis. Fever, leukocytosis and roentgen findings are significant but vary in the degree to which they contribute to diagnosis.

Although no new diagnostic methods are available, success will increase with the completeness of the procedure outlined above.[7] If history is sketchy and does not bring out the constancy of pain, if rectal examination is omitted, if physical examination is done only once, the patient may be dismissed with a diagnosis of gastroenteritis.

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REFERENCES

1. Brayton, D., and Lewis, Jr., G. B.: The use of hypothermia in general pediatric surgery; a preliminary report, Ann. Surg., 145:304-310, 1957.

2. Colle, E., and Paulsen, E. P.: Fluid therapy in surgical conditions, Pediat. Clin. No. Amer., 6:155-167, 1959.

3. Gillespie, C. E., and Moore, C. H.: Acute abdominal emergencies in infancy and early childhood, Arch. Surg., 66:841-851, 1953.

4. Hindmarsh, D., and Court, D.: Emergencies in general practice. The acute abdomen in children, Brit. Med. J., 2:899-902, 1955.

5. McCarty, W. R.: The management of the acute abdomen, Med. Clin. No. Amer., May 1957, p. 789-797.

6. McLanahan, S.: Further reductions in the mortality in acute appendicitis in children, Ann. Surg., 131:853, 1950.

7. Requarth, W., and Samuels, Jr., T. W.: Common errors in diagnosis of the acute abdomen, Surg. Clin. No. Amer., Feb. 1958, pp. 227-238.

Synthetic Antimalarial Drug Therapy in Lupus Erythematosus And Polymorphous Light Eruptions

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• **The therapeutic efficacy of the synthetic antimalarial agents in lupus erythematosus and the polymorphous light eruptions is well established. Severe toxic reactions are rare but mild disturbances are relatively common. Although gold therapy probably is as effective in discoid lupus erythematosus, the antimalarials are easier to administer and cause fewer serious side effects. The mechanism of action of these drugs is poorly understood although definite anti-inflammatory properties have been noted. Perhaps further investigations of known biological processes such as free radical formation and neutralization, redox potential alterations or enzymatic changes may shed more light on this problem.**

ANTIMALARIAL DRUGS have been used in the treatment of lupus erythematosus for over sixty years.[37] However, they were not utilized to any extent in the English-speaking countries until 1951, when Page presented his dramatic results with atabrine.[36] Subsequently, the synthetic antimalarials, atabrine, chloroquine, plaquenil, and more recently camoquin, have been shown to be of great therapeutic value not only in lupus erythematosus but also in polymorphous light eruptions.

Since these drugs are readily absorbed from the gastrointestinal tract they are taken orally as a rule, although intramuscular and intravenous preparations are available. Tissue concentrations, especially in the liver, spleen, kidney and lung, greatly exceed plasma levels, probably because of the affinity of the drugs for nuclear material. Apparently the drugs are metabolized in the body and only 10 to 25 per cent of the daily dose is excreted as such in the urine. In addition, measurable amounts remain in the system up to several weeks after cessation of therapy.[2,3,6,43]

Most patients with discoid lupus erythematosus respond to adequate doses of any of the synthetic antimalarial drugs previously mentioned. Improvement usually is seen in the first four to six weeks of treatment and may be maintained and enhanced by continuing on relatively low doses. However, relapses are quite common, occurring in up to 80 per cent of patients within the first year and frequently appearing a few weeks after discontinuance of atabrine or chloroquine. The disease usually responds promptly on resumption of the same drug, although occasionally another antimalarial agent must be substituted to bring the condition under control.[11,27,38] No adequate statistics are available as yet for the relapse rate after plaquenil or camoquin therapy.

Table 1 gives comparisons of the effective doses of the synthetic antimalarials now used in lupus erythematosus. For the most part they are interchangeable, although at times a certain one will be more effective or less toxic for a specific individual. The dosage schedules vary with the patient's therapeutic response and toxic reactions. In an average course for an adult, 250 mg. of chloroquine (or the equivalent amount of one of the other antimalarials) is given twice a day for one to four weeks. The dose is then reduced to a maintenance level, usually 250 mg. a day. It should be noted that children appear to tolerate these drugs well and the dosage can be calibrated to correspond to a 70 kilogram adult. Christiansen's studies indicate that the patient should receive 25 gm. of atabrine before therapy can be considered unsuccessful. Also, he found very little additional improvement with giving more than this amount.[11] However, other workers noted that more prolonged treatment, with chloroquine at least, appreciably reduced the relapse rate.[13] It may prove to be of value to continue low dose therapy such as 250 mg. of chloroquine one to four times a week for several months after remission of the disease.

Sex, duration of the disease or character of the lesions apparently do not influence the outcome of the therapy, although the active erythematous plaques usually respond more rapidly. Oral lesions are quite resistant to treatment. There is some evidence that patients over 60 years of age are more successfully treated than younger persons.[11]

It should be emphasized that the antimalarial drugs are of value in systemic as well as discoid lupus erythematosus. Dubois[15] found that 80 per cent of patients with milder systemic changes responded to these drugs alone and that the steroid dosage could be considerably reduced when the agents were used concurrently.

The response of the polymorphous light eruptions

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TABLE 1.—*A Comparison of Average Dose Schedules for Different Synthetic Antimalarial Agents*

Drug	Usual Tablet Size	Daily Dose
Atabrine (Mepacrine, Quinicrine)	100 mg.	100 to 300 mg.
Chloroquine (Aralen, Nivaquine)	250 mg.	250 to 750 mg.
Plaquenil (WIN 1258)	200 and 400 mg.	400 to 1200 mg.
Camoquin (Amodiaquin)	200 mg.	200 to 400 mg.
Triquin (APA 5533)	*	1 to 5 tablets

*Triquin contains Aralen 65 mg., Plaquenil 50 mg., and Atabrine 25 mg.

is as dramatic as that noted with lupus erythematosus. The dosage schedules are similar although, in my experience at least, smaller amounts are needed for the light eruptions. Treatment usually must be continued throughout the summer and must be restarted the next spring.

Although the synthetic antimalarial agents are considered by most investigators to be the drugs of choice in these two diseases, Crissey and Murray found no significant difference between the results of gold and chloroquine therapy of discoid lupus erythematosus. The number of relapses was actually higher with the short term chloroquine treatment but more prolonged therapy reduced this recurrence rate.[13] The antimalarial agents do have the advantage of ease of administration and a lower incidence of disabling adverse reactions.

Although these drugs are not without some danger, severe toxic effects are quite rare. In humans, atabrine toxicity essentially is limited to the gastrointestinal tract, central nervous system, eyes, bone marrow, skin and liver. The most serious reactions include (1) liver damage, at times associated with exfoliative dermatitis, corneal edema and aplastic anemia; (2) agranulocytosis and aplastic anemia often preceded by the so-called "New Guinea lichen planus"; (3) toxic psychosis and (4) permanent blindness. The cutaneous alterations range from allergic erythema mutiforme to toxic or allergic lichenoid and exfoliative changes.[2,14,19,40] Anhidrosis due to deposition of the drug in the distal part of the sweat ducts resulted in a sweat retention syndrome in the South Pacific.[22] It should be noted that, in a long term study, Agress found less than a 0.05 per cent incidence of serious toxic reaction to atabrine.[2] Atabrine is seldom used nowadays, chiefly because of the cosmetically unacceptable yellow discoloration which occurs in most patients taking the drug for more than a week.

No skin discoloration, hepatic damage, significant bone marrow depression or hematopoietic system changes have been reported with chloroquine, although occasionally leukopenia and methemoglobinemia have been noted.[4] Mild central nervous system and visual disturbances are not uncommon; depigmentation of red and blond hair, and yellow discoloration of white hair may occur.[3,10,18] Gastrointestinal toxicity is usually mild, although hematemesis has been observed.[24] Skin reactions, both allergic and toxic, have been reported.[3,4] Although the untoward reactions to this drug almost always have been reversible, permanent atrophy of the macula was noted recently.[40]

Apparently plaquenil produces less undesirable side effects and camoquin is considered by some observers to be the least toxic of all of these agents. However, certain ocular, central nervous system, gastrointestinal, hematopoietic and hepatic changes have been reported with one or both of these drugs and further observations may alter our present benign feelings toward them.[5,7,27] It is interesting but not unexpected that plaquenil, which is a hydroxychloroquine derivative, has caused hair depigmentation and that camoquin, a yellow powder, has produced skin discoloration not unlike that seen with atabrine.[7,30,45] Recently triquin, a combination of relatively small amounts of chloroquine, atabrine and plaquenil, has been tried in an effort to reduce the amount of side effects as well as to increase the efficacy of this type of therapy. It has been under investigation for too short a time for definitive evaluation.

In addition to the above-mentioned untoward effects of the synthetic antimalarials, there are certain conditions in which these drugs are contraindicated. In patients with psoriasis severe exfoliative states are induced, and in patients with porphyria acute attacks may be precipitated. It also seems reasonable that the drug should be used with caution in patients with hematopoietic or liver disturbances.

The mechanism (or mechanisms) of action of these drugs is not well understood. The various theories and approaches that have been postulated and investigated are listed below:

1. Light filtration
2. Antibody inhibition
3. Anti-inflammatory
   a. Enzymatic
      (1) Antihyaluronidase
      (2) Anticholinesterase
      (3) Oxidative phosphorylation
      (4) Antiadenotriphosphatase
   b. Adenosine inhibition
   c. Nucleoprotein binding

d. Pituitary adrenal system
e. Local effect.

Although the antimalarial agents do alter at least certain responses to ultraviolet in lupus erythematosus and the polymorphous light eruptions, the bulk of evidence at present is against the supposition that the main therapeutic effect comes from a sun-screening action.[9,44] Also, at this time there is no evidence to indicate any specific effect on antibody production or antigen-antibody reactions.

Experimental studies have shown that the synthetic antimalarial drugs produce an increased latent period and a decreased intensity of phenol induced erythemas, an acceleration of ulcer healing, a decreased inflammation and blood vessel permeability and a decided antihyaluronidase action.[8,28,42] How these anti-inflammatory effects are brought about is not clear. The antihyaluronidase activity is less pronounced in humans than in animals.[29] Binding of cholinesterase and anticholinergic-like actions have both been reported.[1,39] Neither of these properties satisfactorily explains the inhibitory effect of the drugs on inflammation.

Haydu[23] postulated that chloroquine may act by means of adenosine triphosphatase inhibition. His theory was based on the apparent increased needs of adenosine triphosphate in rheumatoid arthritis, the adenosine triphosphate-sparing action of drugs in the quinine group and the demonstration that atabrine can reversibly uncouple phosphorylation and oxidation reactions.[23,31] Recent observations by Findlay[17] indicated that quinine, atabrine and chloroquine do not affect adenosine triphosphatase. Other investigators have suggested that the antimalarial agents act by antagonizing the physiological actions of adenyl derivatives since the effects of adenosine triphosphate on heart muscle are inhibited by these drugs. This is not a specific antagonism of adenosine triphosphate or the adenyl groups.[21]

The binding of nucleoproteins by the antimalarial drugs probably accounts for the high tissue concentrations of these agents and for the inhibitory effect they have on the *in vitro* lupus erythematosus cell test. Whether this action is of importance in preventing *in vivo* changes is unknown.

More recently, the influence of the synthetic antimalarial agents on adrenal cortical steroid metabolism has received considerable attention. Nagy and Kocsár[32] found an increase in urinary 17 ketosteroids in humans taking atabrine. In contrast, Lapiere and Cauwenberge[26] noted low 17 ketosteroid excretion and high 17 hydroxycorticoid levels in the plasma and urine associated with chloroquine therapy. Also, Nagy and his co-workers found hypertrophy and evidence of increased secretory activity of the adrenal cortices of animals following prolonged atabrine intake.[33] Neither the studies of the present author and co-workers[16] nor those of Shelley and Arthur[39] substantiated these preliminary reports of increased blood and urinary 17 hydroxy or 17 ketosteroids. In addition, in an extensive investigation of chronic chloroquine toxicity in rats, Nelson and Fitzhugh[34] noted that the adrenal glands were normal except for changes due to inanition.

At present we are investigating the anti-inflammatory actions of intradermally injected antimalarials. We have been able to confirm the beneficial effects on resistant plaques of lupus erythematosus noted by Thies and others.[35,41] Our studies suggest that at least part of this action may be due to a nonspecific toxic effect.

The foregoing discussion has emphasized that the antimalarials are quite effective in suppressing the abnormal inflammatory reactions related to lupus erythematosus and polymorphous light eruptions. The mechanism of this effect is still poorly understood. Recent studies have suggested that lack of reducing substances or an excess of activated oxygen plays an important role in photosensitivity reactions.[25] In addition, the relationship of free radical formation to biological oxidation-reduction reactions, and photo-activation has received considerable attention.[12] Perhaps further investigations related to free radical neutralization or reduction of activated oxygen would shed more light on the mechanism of action of these drugs.

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ADDENDUM

Since this account was prepared, an extensive report of deposits of opaque material in the cornea of patients taking chloroquine has been published. (Hobbs, H. E., and Calnan, C. D.: Visual disturbances with antimalarial drugs, with particular reference to chloroquine keratopathy, Arch. Derm., 80: 557-563, Nov. 1959.)

REFERENCES

1. Agarwal, S. L., and Arora, R. B.: Anticholinergic actions of chloroquine and camoquin on smooth and cardiac muscles, Indian J. M. Research, 44:631-636, 1956.

2. Agress, C. M.: Atabrine as a cause of fatal exfoliative dermatitis and hepatitis, J.A.M.A., 131:14-21, 1946.

3. Alving, A. S., Eichelberger, L. C., Craige, B., Jr., Jones, R., Jr., Whorton, C. M., and Pullman, T. N.: Studies on chronic toxicity of chloroquine, (SN—7618), J. Clin. Invest., 27:60-65, 1948.

4. Ayres, S., III, and Ayres, S., Jr.: Chloroquine in treatment of lichen planus and other dermatoses, J.A.M.A., 157:136-138, 1955.

5. Bennett, J. H., and Rees, R. B.: Plaquenil sulfate in treatment of lupus erythematosus and light-sensitivity eruptions, A.M.A. Arch. Dermat., 75:181-183, 1957.

6. Berliner, R. W., Earle, D. P., Jr., Taggart, J. V., Zubrod, C. G., Welch, W. J., Conan, N. J., Bauman, E., Scudder, S. T., and Shannon, J. A.: The physiological disposition, antimalarial activity, and toxicity of several derivatives of 4-aminoquinoline, J. Clin. Invest., 27:98-107, 1948.

7. Bleil, D. C.: Unusual toxic manifestations to amodiaquine, A.M.A. Arch. Dermat., 77:106-107, 1958.

8. Blaich, W., and Gerlach, V.: Mechanism of effect of chloroquine on lupus erythematosus, Hautarzt., 6:267-270, 1955.

9. Cahn, M. M., Levy, E. J., and Schaffer, B.: Polymorphous light eruption: The effect of chloroquine phosphate in modifying reactions to ultraviolet light, J. Invest. Dermat., 26:201-207, 1956.

10. Calkins, L. L.: Corneal epithelial changes occurring during chloroquine therapy, A.M.A. Arch. Ophth., 60:981-988, 1958.

11. Christiansen, J. V., and Nielsen, J. P.: Treatment of lupus erythematosus with mepacrine, Brit. J. Dermat., 68:73-87, 1956.

12. Commoner, B., Townsend, J., and Pake, G. E.: Free radicals in biological materials, Nature, 174:689-691, 1954.

13. Crissey, J. T., and Murray, P. F.: A comparison of chloroquine and gold in the treatment of lupus erythematosus, A.M.A. Arch. Dermat., 74:69-72, 1956.

14. Custer, R. P.: Aplastic anemia in soldiers treated with atabrine, Am. J. Med. Sci., 212:211-224, 1946.

15. Dubois, E. L.: Systemic lupus erythematosus: Recent advances in its diagnosis and treatment, Ann. Int. Med., 45:163-184, 1956.

16. Epstein, J. H., Forsham, P. H., and Friedman, E.: Effect of chloroquine on adrenal corticoid metabolism, J. Invest. Dermat., 32:109-114, 1959.

17. Findlay, G. H.: Light eruptions and the A. T. P. mechanism, Brit. J. Dermat., 70:242-244, 1958.

18. Gold, S.: Hyperpigmentation of hair following chloroquine (case presented at the Roy. Soc. of Med.), Brit. J. Dermat., 70:378, 1958.

19. Goodman, L. S., and Gilman, A.: The pharmacological basis of therapeutics, Second Ed., New York, The Macmillan Co., 1955, pp. 1161-1207.

20. Granirer, L. W.: Exfoliative dermatitis as a complication of chloroquine therapy in rheumatoid arthritis, A.M.A. Arch. Dermat., 77:722-724, 1958.

21. Green, H. N., and Stoner, H. B.: Biological actions of adenine nucleotides, London, H. K. Lewis and Co., Ltd., 1950, pp. 188-196.

22. Herrmann, F., and Miller, O. B.: Pharmacologic and pathogenetic effects of mepacrine chloride upon the human skin, I. Clinical and experimental observations, Acta Dermat. Venerol., 32:304-316, 1952.

23. Haydu, G. G.: Inhibition of adenosintriphosphatase activity in rheumatoid arthritis, Rheumatism, 10:32-34, 1954.

24. Harvey, G., and Cochrane, T.: The treatment of lupus erythematosus with chloroquine sulphate, J. Invest. Dermat., 22:89-91, 1954.

25. Langhof, H., and Muting, D.: Amino acid metabolism and BAL therapy of light dermatoses, Hautarzt., 6:27-28, 1955.

26. Lapiere, S., and Cauwenberge, H.: The effect of chloroquine treatment on the corticosteroid content of blood and urine in a case of acute systemic lupus erythematosus, Arch. Belg. Derm. Syph., 12:1-9, 1956.

27. Leeper, R. W., and Allende, M. F.: Antimalarials in the treatment of discoid lupus erythematosus, A.M.A. Arch. Dermat., 73:50-57, 1956.

28. Leoni, A.: Effects of chloroquine in erythematosus reaction to phenol in patients with chronic lupus erythematosus, Minerva Dermat., 30:410-411, 1955.

29. Leoni, A., Marson, G., and Rossetti, C.: Experiments on mechanism of action of chloroquine; action of chloroquine on phenomena of diffusion, Minerva Dermat., 31:261-263, 1956.

30. Lewis, H. M., and Frumess, G. M.: Plaquenil in the treatment of lupus erythematosus, A.M.A. Arch. Dermat., 73:576-581, 1956.

31. Loomis, W. F., and Lipmann, F.: Reversible inhibition of the coupling between phosphorylation and oxidation, J. Biol. Chem., 173:807-808, 1948.

32. Nagy, E., and Kocsár, L.: Untersuchungen über die antihistaminartige wirkung des atebrins, Derm. Wschr., 133:265-267, 1956.

33. Nagy, E., Kocsár, L., Jokay, I., Hadhazy, C., and Tuza, K.: Nevere daten zum wirkungsmechanismus des atebrins, Dermatologica, 115:143-148, 1957.

34. Nelson, A. A., and Fitzhugh, O. G.: Chloroquine (SN—7618): Pathologic changes observed in rats which for two years had been fed various proportions, Arch. Path., 45:454-462, 1948.

35. Ottolenghi-Lodigiani, F.: Local intradermal application of acridine preparations for treatment of chronic lupus erythematosus, Hautarzt., 6:24-27, 1955.

36. Page, F.: Treatment of lupus erythematosus with mepacrine, Lancet, 2:755-758, 1951.

37. Pillsbury, D. M., and Jacobson, C.: Treatment of chronic discoid lupus erythematosus with chloroquine, J.A.M.A., 154:1330-1333, 1954.

38. Rogers, J., and Finn, O. A.: Relapse in discoid lupus erythematosus treated with antimalarial drugs, A.M.A. Arch. Dermat., 74:387-388, 1956.

39. Shelley, W. B., and Arthur, R. P.: The failure of chloroquine to stimulate the human adrenal cortex, J. Invest. Dermat., 31:109-114, 1958.

40. Sternberg, T. H., and Laden, E.: Discoid lupus erythematosus: Bilateral macular degeneration due to chloroquine, Soc. Trans., A.M.A. Arch. Dermat., 79:116-118, 1959.

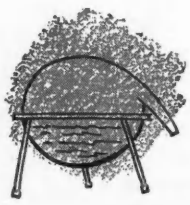
41. Thies, W.: Recent experiences in treatment of chronic discoid lupus erythematosus with atabrine and chloroquine, particularly with local and combined therapy, Hautarzt., 6:227-232, 1955.

42. Whitehead, R. W., and Hager, J. P.: The anti-inflammatory and anti-hyaluronidase effects of chloroquine, J. Pharm. and Exper. Therap., 110:52-53, 1954.

43. Wiselogle, F. Y. (Ed.): Survey of antimalarial drugs, Vol. I, 1941-45, Ann Arbor, Michigan, J. W. Edwards, 1946, 99-104.

44. Wiskemann, A., and Koch, H.: Experimental and clinical studies on mode of action of atabrine and chloroquine in chronic lupus erythematosus, Hautarzt., 9:215-218, 1958.

45. Young, E.: Melanosis caused by camoquin, Dermatologica, 116:389-395, 1958.



8-Methoxypsoralen

A Short Review and Comment

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• **8-Methoxypsoralen is a purified extract of the root *ammi majus lynn*, which was used in a crude form for centuries in the Middle East in the treatment of various skin diseases. In recent years it has been found that the purified extract, when taken internally, increases all skin responses to sunlight, including tanning. When too much drug is taken or when the patient is exposed to sunlight too long, the preliminary erythema may be painful, and blistering may occur. In some patients with vitiligo, islands of pigmentation appear around the hair follicles when the drug is taken, and in favorable cases these islands may coalesce to form continuous areas of pigmented skin. The drug has been found nontoxic, but successful treatment of vitiligo takes place in only a small proportion of patients.**

Promiscuous use of the drug for cosmetic tanning is to be deplored. The constant irritation of the skin due to the increased action of sunlight when the drug is used may possibly increase the incidence of sun-induced skin cancers.

A topical preparation is available, which, when used with great care, may help to repigment small areas of vitiligo.

IN ANCIENT TIMES, many skin diseases were regarded as forms of leprosy. Because leukodermia is often seen in Hansen's disease, it is probable that fear of being shunned as lepers prompted sufferers from vitiligo to use oral and topical preparations of the plant *Ammi majus Linn*, which grows along the Nile. The crude preparation taken by mouth was reputed to cause many serious side effects, the most significant being liver damage. In 1947, two Egyptian biochemists, Fahmy and Abu-Shady,[4] isolated the most active principles from the plant and found them to be furocoumarins—highly photosensitizing compounds. One of these, 8-methoxypsoralen (8-MOP) is the main constituent of the extract.

Until the discovery of 8-MOP no satisfactory treatment for vitiligo existed. The new preparation was eagerly investigated and within a short time a plethora of enthusiastic papers was forthcoming. Work has been almost continuous and the purpose of this short paper is to summarize the more clinical aspects of these efforts. The comments will be my own and may not entirely agree with those of other investigators.

There is no doubt that 8-MOP in some way increases sun tanning. In the normal skin of dark persons a rich tan is produced, and with care moderate tanning will take place in the fair skinned and even in redheads. In vitiligo, as is well known, pigment production upon use of this drug commences in follicular islands (Figure 1), and in favorable cases these islands coalesce to form unbroken areas of pigment. Unfortunately, the treatment is tedious and often frustrating. While in some patients new pigment formation becomes obvious in as short a time as two weeks, in most cases several weeks and even months of therapy is necessary before repigmentation commences. Moreover, in many patients follicular islands may appear but never join with one another; some persons may completely repigment in certain areas and not produce any new melanin in others; and finally, even

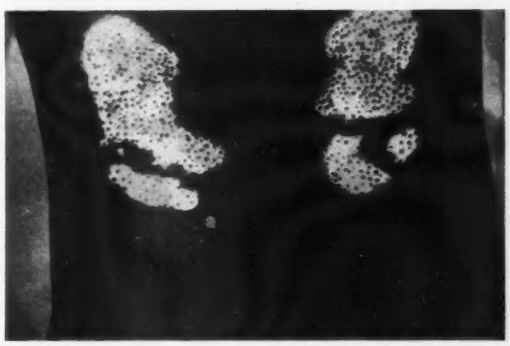

Figure 1.—Good follicular response about the knees to 8-MOP.

in successful cases the new pigmentation may fade after treatment is stopped. In a recent paper Levai[5] commented on the sites in which treatment is more likely to be successful. Taking complete repigmentation as the only criterion (for obviously partial follicular repigmentation is cosmetically as undesirable as vitiligo) the treatment has been effective in

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perhaps 30 per cent of cases in which I have used it. Even this relatively small success is an advance.

In an effort to save the unfortunate majority of patients expense and inconvenience by attempting to forecast success or failure at the first interview, certain criteria may be noted. Speaking generally, the older the vitiligo the worse the prognosis. Many patients will show follicular islands of melanin at the first examination, and these are presumably of favorable significance. A theory that is deserving of more attention is that put forward by Pegum.[7] He noted that the work of Billingham and Medawar[2] established that in man and certain animals two distinct melanocyte systems exist, one in the basal layer and one in the hair apparatus. These are anatomically distinct because the melanocytes of the basal layer surround the neck of the hair follicle but do not run down to the hair bulb, where another group of melanocytes is found. Physiologically, they are demonstrably distinct because one may find dark hairs in white skin in man, and red hairs in black skin in guinea pigs; and using cell suspensions and a microcannular technique, black melanocytes can be introduced into red or white hair follicles and result in the growth of black hairs. Billingham and Medawar removed areas of skin in Thiersch-graft thickness from guinea pigs, thus removing the melanocytes in the basal layer, and found that skin would regenerate entirely from the intact hair bulbs, with the pigment cells derived from the hair follicles also.

Using this work as a guide, Pegum attempted to treat vitiligo by removing epidermis in several ways. He took a Thiersch-graft thickness in two patients, blistered other vitiligo areas with carbon dioxide snow, and with cantharidin, and in other ways attempted to get rid of the inactive basal melanocytes. In several of these experiments, repigmentation from the hair follicles resulted. Correlating this work with the reports of follicular repigmentation taking place with 8-MOP therapy, he suggested that in an area of vitiligo where the hairs are pigmented a good result with 8-MOP may be anticipated. Conversely, if the hairs are white and depigmented (Figure 2) the prognosis is poor.

Much has been written regarding the possible toxic effects of psoralen. Transient changes in liver profile studies have been reported but in some of these there were no pretreatment studies.[3] In the others the abnormalities have quickly reversed following termination of treatment. Two cases of jaundice proved to be of viral origin. There have been four reports of development of light sensitivity in previously normal persons.[9] Five patients noted muscular incoordination which disappeared when they no longer took the drug.[10] No report of serious toxicity has yet been forthcoming in a collection of literature which must surely cover many hundreds of cases.

Figure 2.—Vitiligo of eyelid showing depigmented lashes. There was no response to treatment with 8-MOP.

Tucker[11] recently thoroughly evaluated this aspect of psoralen therapy in an excellent review. No drug has been more maligned than 8-MOP on this score and none more thoroughly investigated and exonerated. To my mind, the danger in 8-MOP therapy consists in the hazards associated with sunburning. Even when the skin is tanned, any intensive period of sun exposure after taking the drug produces erythema beneath the tan, and a sensation of burning. Although it has been suggested that 8-MOP could be used to produce a protective tan in patients prone to form basal cell carcinomas, it has been my feeling that it will potentiate the formation of skin cancer—as it does all the other effects of sunlight. Thus, it is interesting to note that Stegmaier[8] reported the case of a 36-year-old male with no previous history of skin cancer who spent two weeks in the Colorado mountains while taking 8-MOP and who developed a basal cell carcinoma of the skin two months later.

It was originally assumed that the tanning action of the psoralens (see Figures 3 and 4) was due to increased melanogenesis and that the resultant heavy pigmentation afforded the sun-protection. A problem was to explain the protection claimed by some albino patients. Here we felt that the shielding must have been due to increased thickening of the skin, as suggested by European workers, notably Miescher.[6] This theory was not satisfactorily demonstrated until recently, when Becker[1] and later Zimmerman[12] produced experimental thickening of the skin following the ingestion of 8-MOP and ultraviolet irradiation. This thickening seems to be due partly to the formation of a stratum lucidum and partly to a lessening of shedding of the stratum corneum due to an increased cohesion of squamous cells. Melanin granules accumulate in the thickened

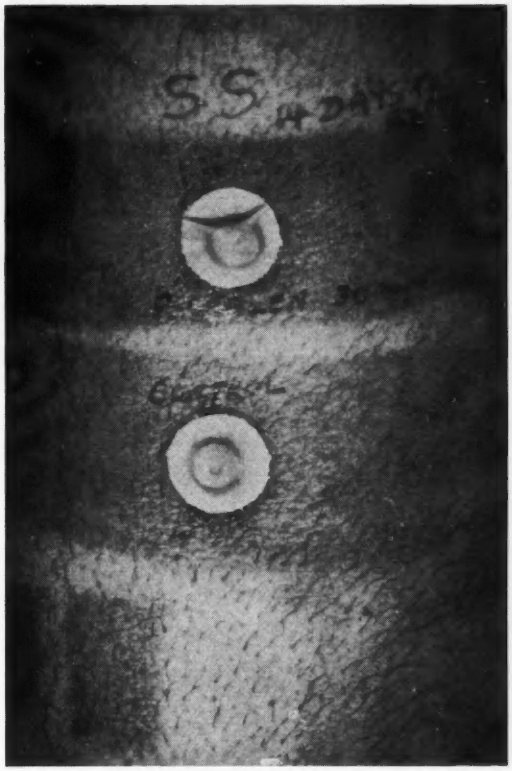

Figure 3.—Increased tanning following single one-hour exposure to sunlight after administration of 30 mg. of psoralen. Lower rectangle is control site.

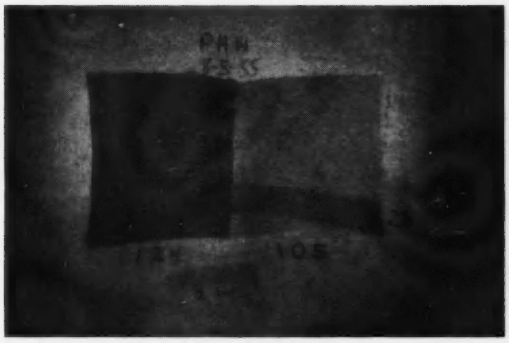

Figure 4.—Remarkable tanning effect of 8-MOP is demonstrated by this experiment in which the squares 124 and 105 were separately exposed to sunlight on alternate days. Square 124 was exposed following ingestion of 8-MOP, and 105 was control square.

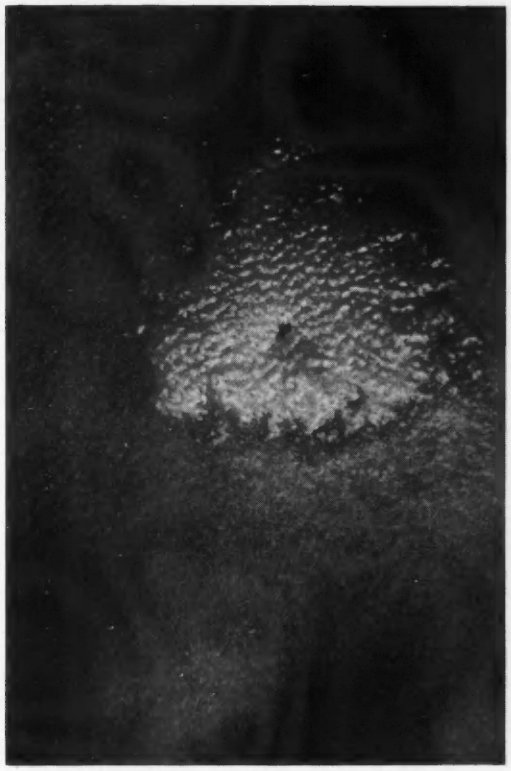

Figure 5.—Blistering following topical application of 8-MOP and excessive sun exposure.

stratum corneum and thus it darkens. A coincidental specific effect on melanogenesis has not been ruled out.

When treating a patient with vitiligo the problems associated with 8-MOP should be emphasized. The patient should be warned both as to length of treatment and the limited chances of success. It is my practice to stress that at first the vitiligo will be more obvious and indeed other patches of vitiligo may become apparent as the normal skin acquires the characteristic tan. The historical hazards of the treatment should be discussed, and a bromsulphthalein liver test should be carried out before treatment and periodically during therapy. The treatment should be commenced early in the summer to allow maximum time for repigmentation to occur. I have found that even in Southern California the sunlight is not strong enough to produce a good result in winter (even in the absence of smog) and that artificial ultraviolet light is not a good substitute for natural sunlight.

Finally, the patient is given thorough instruction regarding taking the drug. Twenty milligrams is the standard dose and should be exceeded rarely. Nausea, flatulence, burning in the throat and water brash are not uncommon and may sometimes be avoided by taking the capsules with a cookie and some milk. Sun exposure should be cautious and increased gradually; and in order to avoid medico-legal com-

plications detailed precautions regarding graduated sunbathing time are written on each prescription.

The topical preparation is potent and difficult to remove completely. Sloppy attempts at removal may wash some of the preparation onto surrounding skin and produce extensive burning after the next sun exposure (Figure 5). However, it may be used with caution on small areas of vitiligo.

Many physicians are afraid of using 8-MOP. In this regard it may be pointed out that there are many widely used drugs with dangerous potentialities. Penicillin is a good example. We do not forbid cigarettes because they may produce a carcinoma of the bronchus. Should we then condemn the psoralens because they may one day potentiate a relatively harmless skin cancer? The furocoumarins are abundant in many fruits and vegetables. An average celery stalk may contain over 1 milligram of psoralens. Used with understanding, 8-MOP has a place in the practice of dermatology.

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REFERENCES

1. Becker, S. W., Jr.: Methods of increasing skin pigmentation, J. Soc. Cosmet. Chem., 9:80-86, March 1958.
2. Billingham, R. E., and Medawar, P. B.: Pigment spread and cell heredity in guinea-pig's skin, Heredity, 2:29-47, June 1948.
3. Elliott, J. A., Jr.: Treatment of vitiligo with 8-methoxypsoralen, So. Med. J., 49:691-697, July 1956.
4. Fahmy, I. R., and Abu-Shady, H.: Isolation and properties of ammoidin, ammidin and majudin and their effect in treatment of leukodermia, Quart. J. Pharm. and Pharmacol., 21:499-503, Oct.-Dec. 1948.
5. Levai, M.: Treatment of vitiligo with psoralen derivatives, A.M.A. Arch. Dermat., 78:597-606, Nov. 1958.
6. Miescher, G.: Das Problem des Lichtschutzes und der Lichtgewoehnung, Strahlentherapie, 35:403-443, Feb. 1930.
7. Pegum, J. S.: Dissociated depigmentation in vitiligo. Significance and therapeutic implications, Brit. J. Dermat., 67:348-350, Oct. 1955.
8. Stegmaier, O. C.: Use of methoxalen in sun tanning, J. Invest. Dermat., 32:345-349, Feb. 1959.
9. Tucker, H. A.: Personal communication.
10. Tucker, H. A.: Personal communication.
11. Tucker, H. A.: Clinical and laboratory tolerance studies in volunteers given oral methoxalen, J. Invest. Dermat., 32:277-280, 1959.
12. Zimmerman, M. C.: Histologic changes in irradiated skin after ingestion of 8-methoxypsoralen, J. Invest. Dermat., 32:269-271, Feb. 1959.

CORRECTION—3,178 gm., not 2,178

A TYPOGRAPHICAL ERROR that changed the purport of the sentence in which it appeared was made in the article "Pulmonary Hyaline Membrane Disease—The Obstetrician's Point of View," by Edward B. Cantor, M.D., which appeared in the January, 1960, issue of this journal.

On page 8, column 2, line 22 the weight of the infant was printed as 2,178 gm. It should have been 3,178 gm.

Synthetic Oxytocin

LESTER T. HIBBARD, *M.D.*, and
ALAN V. ANDREWS, *M.D.*, Los Angeles

• **A synthetic oxytocin, Syntocinon®, was used in 3,342 obstetrical patients for a wide variety of indications. It was concluded that the preparation is as effective as natural oxytocin.[1] There were no side effects observed, particularly vasospasm or anaphylactic reaction. Its use in clinical obstetrics can be recommended provided there is a proper indication for its use and the need for close supervision and individual adjustment of dosage is recognized.**

THE UNIQUE VALUE of posterior pituitary extracts in obstetrical practice lies in their ability to stimulate physiological, effective uterine contractions. Because the oxytocic principle contained in these preparations is an extremely potent drug, they have been both admired and feared. The very potency which affords numerous uses of oxytocin in normal and abnormal obstetrical situations is capable, if injudiciously employed, of producing serious and even fatal accidents.

In recent years, however, better preparations of oxytocin, better methods of administration and better appreciation of proper safety precautions, have combined to enhance the value of these drugs and to increase their range of usefulness.

Recently, as a result of several investigations, oxytocin has been synthesized. In 1953, the chemical structure of oxytocin was elucidated almost simultaneously by DuVigneaud and associates in the United States and Tuppy in Austria. In the following year, DuVigneaud was able to synthesize oxytocin and, in 1955, Boissonnas evolved a method of manufacturing synthetic oxytocin on a commercial scale.[2] Now synthetic oxytocin—manufactured by the Sandoz Company under the trade name Syntocinon®—is available for clinical use.

Extensive clinical testing indicates that synthetic oxytocin is a valuable drug.[3,4,8,9] Not only does it produce oxytocic effects identical to purified posterior pituitary extract, but also it possesses the following desirable features: (1) uniform potency, (2) freedom from animal protein, and (3) freedom from vasopressor substances capable of producing alterations in blood pressure or coronary artery circulation.[10,13,14,15]

PRESENT STUDY

In order to test its clinical usefulness, synthetic oxytocin was administered to 3,342 patients at the Los Angeles County General Hospital for a wide range of indications and employing the following dosage schedules:

1. Intramuscularly to stimulate labor: One-half unit (1/20 cc.) repeated as necessary at 20-minute intervals.

2. Intramuscularly before the delivery of the placenta: 10 units (or 1 cc.).

3. Intravenously with the birth of the anterior shoulder: 10 units undiluted.

4. Intravenous infusion to control postpartum hemorrhage or uterine atony: 30 or 40 units in 1,000 cc. of 5 per cent dextrose in water.

5. Intravenous infusion to stimulate labor: 5 units in 500 cc. of dextrose in water or, if the uterus appeared to be particularly irritable, 3 units in 500 cc. of 5 per cent dextrose in water.

When Syntocinon® was administered by intravenous infusion during labor, a physician or experienced nurse was present at all times to observe the strength and frequency of uterine contractions. When the observer was a nurse, the physician remained in the hospital and close at hand. This is essential because both the optimal and safe rates of administration are variable and depend entirely on the initial and continued response of the individual patient. Ordinarily, the rate of infusion was started at 8 to 10 drops a minute and varied according to the subsequent uterine response. The range of variation was between 6 and 60 drops a minute. As labor progressed, the rate of flow was altered, as necessary, to maintain uterine contractions at three- to five-minute intervals. Rarely was the infusion discontinued during labor, unless contractions became quite strong. If there was any element of uterine inertia, infusion was continued through delivery into the postpartum period in order to avoid uterine atony. Initial strong, prolonged uterine contractions which suggested tetany made it necessary to discontinue infusion in three instances. Subsequently, one patient went into spontaneous labor, and the

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infusion was restarted in the other two patients without further complications.

When Syntocinon® was given by intravenous infusion, the following contraindications were observed: Previous uterine scar; transverse or compound presentation; definite cephalopelvic disproportion; abnormal fetal heart tones, grand multiparity (over para-five) (unless complications of pregnancy demanded induction, for example, diabetes or toxemia).

Judging from recent reports, the exact indications for oxytocin are a controversial matter.[7,11] There are those who find a wide range of clinical application and others who would limit its use. We wished to test a broad range of indications, listed as follows:

1. Elective induction of labor.
2. Indicated or therapeutic induction of labor.
3. Elective acceleration of labor.
4. Indicated or therapeutic acceleration of labor.
5. Acceleration of the delivery of the placenta.
6. Prophylaxis and treatment of uterine atony.
7. Completion of inevitable abortion, incomplete abortion and hydatidiform mole.

RESULTS

Elective induction of labor: A number of reports recommend oxytocin by intravenous infusion for the elective induction of labor.[6,16] It has been said that when cases are properly selected, the procedure is better than 97 per cent effective, with or without artificial rupture of the membranes.[5] Providing that the membranes have not been ruptured, there has been no adverse effect on either the mother or the fetus. In this series, induction of labor was elected in 108 cases utilizing the following criteria:

(a) The patient was at term as judged by menstrual history and fetal development.

(b) The uterus was irritable.

(c) The presenting part filled the pelvis and fitted against the lower uterine segment.

(d) The cervical os was either anterior or in the axis of the vagina.

(e) There was evidence of cervical softening with beginning dilatation and effacement.

The membranes had been ruptured before the start of the intravenous infusion in 70 cases and unruptured in 28 cases. There seem to be two advantages in starting the infusion before amniotomy. First, the subsequent amniotomy is easier; and, second, observed dilatation and effacement of the cervix makes one more certain the pregnancy is at term. If the cervix does not change in a reasonable period, the infusion may be discontinued without jeopardy to mother or child. Observing the above technique, the rate of flow was increased or decreased in order to maintain the proper pattern of uterine contractions. Of the 108 patients, 106 were delivered during the initial infusion. One of the two remaining patients was delivered during the second course of intravenous oxytocin, and the other 12 hours after the second course was completed. There were no adverse effects noted either on the mother or the infant.

Indicated or therapeutic induction of labor. Induction of labor may be indicated for a variety of reasons. Among those often given are toxemia of pregnancy, diabetes, previous severe erythroblastosis, postmaturity and intrauterine fetal death. To this list might be added ruptured membranes with delayed onset of labor, particularly if amnionitis is feared. Thirty-seven patients falling in this category were given an intravenous infusion with the following results:

1. Ruptured membranes with delayed onset of labor (18 cases). All the patients were within four weeks of term. In every instance, the delivery was successful and infants were born in good condition. The average length of labor was 3 hours and 59 minutes.

2. Toxemia of pregnancy (13 cases). Eleven patients were within four weeks of term and two were within the thirty-ninth week of pregnancy. In each case, it was possible to rupture the membranes before initiation of the intravenous infusion. All infants were delivered vaginally and 11 survived. One 5 pound 2 ounce infant died of the effects of atelectasis and one 6 pound 11 ounce infant died of unknown cause during the course of labor.

3. Diabetes (three cases). The three patients were multigravida and were between the thirty-sixth and thirty-eighth week of pregnancy. In each case a normal living infant was delivered vaginally after rupture of membranes and intravenous infusion of oxytocin.

4. Abruptio-placenta (two cases). In both cases the abruption was severe and no fetal heart tone could be heard before the initiation of intravenous infusion. Vaginal delivery was successful in both cases. One patient required 6 gm. of fibrinogen because of a fibrinogen deficiency manifested by poor clot formation.

5. Marginal placenta previa with delayed onset of labor (one case). The patient entered the hospital near the term of her fifth pregnancy because of painless vaginal bleeding. A diagnosis of marginal placenta previa was made by vaginal examination and the membranes were ruptured. When the patient did not go into labor after six hours of observation, intravenous infusion of oxytocin was begun and vaginal delivery of the living surviving infant occurred two hours later. Blood loss during labor was not excessive and the lower uterine segment remained intact.

Elective acceleration of labor. While oxytocins are unnecessary and not indicated during the course of normal labor, they can be used to accelerate the prodromal stages of labor or labor slowed by too early sedation, and in selected cases of false labor which fit the criteria for elective induction. Fifty-four patients are included in this category:

1. False labor (15 patients). The patients had been admitted to the hospital in false labor. Uterine contractions ceased shortly after admission. Since they were at term by dates and physical examination and since the condition of the cervix was favorable, intravenous administration of oxytocin was initiated. In all cases, effective labor began almost immediately and vaginal delivery ensued. All infants were normal.

2. Prodromal labor (28 patients). The patients were judged to be in the prodromal stages of labor, having been observed for periods ranging from two to twelve hours. Oxytocin was given intravenously to shorten the prodromal stage and in all cases a normal pattern of labor was established, followed by vaginal delivery of a normal infant.

3. Sedation in early labor (11 patients). Uterine contractions were either decidedly slowed or apparently stopped. In all cases, intravenous infusion of oxytocin was effective in reestablishing a normal pattern of uterine contractions, followed by vaginal delivery of a normal infant.

Indicated or therapeutic acceleration of labor. Uterine inertia is usually classified as being either hypotonic or hypertonic.[12] Hypotonic inertia is characterized by weak and ineffective uterine contractions occurring either primarily or secondarily after a period of normal labor. Oxytocins, preferably given intravenously, are clearly indicated for hypotonic inertia. Sixteen patients with primary hypotonic uterine inertia were treated by intravenous administration of Syntocinon.® Fourteen normal infants were successfully delivered vaginally after a normal pattern of uterine contractions was reestablished. Two living infants were delivered by cesarean section when it became evident that there was also an element of cephalopelvic disproportion. Seven patients with secondary inertia were stimulated with intravenous Syntocinon,® four after a period of rest. Six infants were delivered vaginally. Five were normal and one was still-born, having died from the effects of amnionitis. One infant delivered by cesarean section because of cephalopelvic disproportion died in the neonatal period of the effects of amnionitis.

A diagnosis of hypertonic uterine inertia is made in patients having abnormal or incoordinate uterine action, often with the lack of a proper polarity, contractions being strong but ineffective. Sometimes a diagnosis is made of colicky uterus, cervical dystocia or constriction ring dystocia. In this series we were unable to identify any case of abnormal uterine action. Some authorities feel that if the diagnosis can be made, oxytocin is contraindicated because it exaggerates the abnormal action.

Acceleration of the delivery of the placenta. 2,800 patients were given 10 units of Syntocinon® intramuscularly following the delivery of the baby and 0.2 mg. of Methergine® intramuscularly following the delivery of the placenta. In 96 per cent of the cases, the placenta separated within an average of three to seven minutes and was then delivered by simple expression. Estimated blood loss was less than 500 cc. in all but 1.5 per cent of the patients. For the remainder the blood loss was estimated to be between 500 and 800 cc. and two patients were thought to have lost at least 1,000 cc. However, no patient with an estimated blood loss of 500 cc. or more had evidence of shock or excessive postpartum anemia. None required a postpartum transfusion.

Manual removal of the placenta was done in 4 per cent of the cases. In half of these cases the procedure was necessary because of retained placenta. In most instances, the placenta had failed to separate within a reasonable time (which was, on the average, 20 minutes). In the remaining cases of manual removal it was done either in connection with a difficult operative delivery, for inspection of the uterine cavity or because the uterus remained atonic following intramuscular administration of Syntocinon.® The incidence of uterine atony following intramuscular use was 0.7 per cent. In a few cases manual removal was done for the purpose of removing placental fragments not delivered at the time of simple expression. Subsequent curettage for postpartum bleeding was necessary for 0.2 per cent of the patients. At the time of curettage no placental fragments were found.

Forty-one patients were given 10 units of undiluted Syntocinon® intravenously with the delivery of the anterior shoulder of the baby. In all cases, the placenta delivered promptly and blood loss was minimal, ranging between 50 and 100 cc. There were no untoward reactions.

Uterine atony. In addition to Syntocinon® intramuscularly at the time of delivery, 90 patients received Syntocinon® by continuous intravenous drip for the purpose of preventing or controlling uterine atony. Sixty-two patients had actual uterine atony, and in the remaining 28 cases atony was feared because of prolonged labor, over-distention of the uterus, uterine fibroids, etc. Either 30 or 40 units of Syntocinon® were added to 1,000 cc. of 5 per cent dextrose in water. Without exception, intravenous drip maintained a good uterine tone and controlled further vaginal hemorrhage. In no case

was a transfusion needed because of subsequent loss of blood. It was felt that for this purpose intravenous Syntocinon® was far superior to a uterine pack.

Abortion and mole. In two hundred cases, Syntocinon® was used either by continuous intravenous infusion or divided doses of 10 units intramuscularly every hour for three or four doses for the purpose of evacuating the products of conception in cases of inevitable abortion, incomplete abortion or hydatidiform mole. No statistical analysis is offered, but it was concluded that Syntocinon® was at least as effective as natural oxytocin for this purpose.

SIDE EFFECTS

Since synthetic oxytocin contains no vasopressor substances, it should have no effect on the blood pressure. No changes of blood pressure were noted during the course of intravenous infusion when it was checked at ten-minute intervals. Neither was there a rise in blood pressure after intramuscular administration when the blood pressure was checked at a 20-minute interval and at a 60-minute interval. The only patients in whom hypertension was noted were those with clear-cut evidence of toxemia of pregnancy or permanent hypertension.

There was no synergistic action between Syntocinon® and anesthetic agents employed. While the usual anesthetic agent was either ether, given by open drop, or spinal, 23 patients were delivered under cyclopropane without untoward effects. If Syntocinon® is free of vasopressor, then there should be no contraindication to its use with cyclopropane. There were no anaphylactic or other untoward reactions.[1,9]

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Syntocinon® was supplied by Sandoz Pharmaceuticals.

REFERENCES

1. Bainbridge, M. N., Nixon, W. C. W., Schild, H. O., and Smyth, G. N.: Synthetic oxytocin, Brit. Med. J., 1:1133, 1956.

2. Boissonnas, R. A., Guttman, S., Jaquenoud, P. A., and Waller, J. P.: A new synthesis of oxytocin, Helvet. chim. acta, 38:1491, 1955.

3. Bosch, K., and Kaser, O.: The use of oxytocin in the management of child birth, with special reference to the synthetic Syntocinon, Schweiz. med. Wchnschr., 86:229, 1956.

4. Chosson, J., Ruf, H., and Barraud, J. P.: Results obtained with a new oxytocic ots. 68 (Syntocinon®), Bull. Fed. Soc. Gynec. Obst., 8:216, 1956.

5. Clark, B. F.: Pitocin in obstetrics, J. Maine Med. Assn., 48:115, 1957.

6. Cole, J. B.: The induction of labor with its complications that may arise from the use of pituitary extract and pitocin, J. Kentucky State Med. Assn., 54:42, 1956.

7. Donnelly, J. F.: The proper use of posterior pituitary extract in pregnancy, No. Carolina Med. J., 18, 1956.

8. Francis, H. H., and Francis, W. J. A.: Clinical trial of synthetic oxytocin, Brit. Med. J., 1:1136, 1956.

9. Friedman, E. B.: Synthetic oxytocin, Amer. J. Obst. & Gynec., 74:1118, 1957.

10. Goodman and Gilman: The pharmacologic basis of medical practice, 2nd edition, Macmillan, 1955.

11. Hellman, L. M., Kohl, S. G., and Schechter, H. R.: Pitocin 1955, Amer. J. Obst. & Gynec., 73:507, 1957.

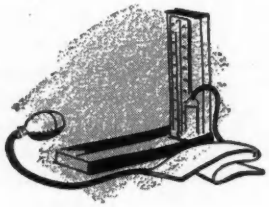
12. Jeffcoate, T. N. A., Baker, K., and Martin, R. M.: Ineffectual uterine action, Surg. Gynec. & Obst., 95:257, 1957.

13. Konzett, H., Berde, B., and Cerletti, A.: Syntocinon®, a synthetic oxytocic post-pituitary hormone, Schweiz. med. wchnschr., 86:226, 1956.

14. Mayes, B. T., and Shearman, R. P.: Experience with synthetic oxytocin: The effects on the cardiovascular system and its use for the induction of labor and control of the third stage, J. Obst. & Gynec. Brit. Emp., 63:812, 1956.

15. Poseiro, J. J., and Caldeyro-Barcia, R.: Effect of synthetic oxytocin on the contractions of the pregnant human uterus. (Effet de l'ocytocine synthetique sur les contractions de l'uterus gravide humain.) Resume of the scientific presentations of the First Reunion of the Latin American Association of Physiologic Sciences, Uruguay, page 6.

16. Ratzan, W. J., and Shulman, A.: Intravenous pitocin and the elective induction of labor, Obst. & Gynec., 6:493, 1955.



Common Granulomatous Inflammations of The Extremities

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• **Granulomatous inflammatory diseases of the extremities caused by inanimate agents (physical or chemical) and agents of unknown character are frequently unrecognized. The symptoms produced by these lesions are too frequently ascribed to trauma, particularly an insignificant bruise or imagined microtrauma. None of the rheumatic diseases—tenosynovitis, myositis, bursitis, fibrositis, gout, rheumatoid arthritis and osteoarthritis—has ever been created by slight or severe mechanical trauma in experimental animals or human beings.**

THE EFFECT of significant actual trauma on the extremities is not obscure or difficult to diagnose. The fundamentals of treatment are universally recognized by physicians and are fairly well comprehended by patients.

One example of significant trauma should suffice to illustrate this: Suppose a closed dorsal dislocation of the wrist occurs. It would be obvious to the patient and the doctor. Suppose, however, that an x-ray film reveals not only the dislocation but a fracture of the lower end of the radius and ulna, which was not obvious to the patient and was not known to the physician before the x-ray; and as usual, all the connecting ligaments are ruptured or torn off the bones, and the extensor tendons are stripped up and the flexor tendons, nerves and blood vessels are stretched taut across the lower end of the ulna—none of which is directly visible to the patient, or the physician by physical inspection. Here, then, is visible and invisible severe significant trauma.

Following the complete reduction of the dislocation as soon as possible to prevent complications of gangrene or permanent nerve injury, what is the expected course of tissue repair in such a case? It progresses steadily toward healing with absorption of hemorrhage and edema, healing of the torn ligaments and fractures, and restoration of the smooth gliding surfaces of the tendons and sheaths, which were so severely traumatized.

After an injury such as this there may be some permanent restriction of wrist motion due to ordinary scar tissue in the ligaments of the wrist, but such a severe injury does not result in the development of ganglion, chronic villous tenosynovitis, bursitis, or calcific densities in the bursae, or stenosing tenosynovitis, or the carpal tunnel syndrome, or chronic traumatic myositis, or rheumatoid arthritis, or osteoarthritis.

The development of these diseases has often been reported as owing to a tear in the ligament of the wrist, bruises, bumps, occupational activity, repetitive motions, use of small hand tools, occupational microtrauma, overstretching of the muscles, exposure to cold—many other extrinsic things.

In this particular example a complication may occur, occasionally seen after a Colles fracture also—and that is that after about six weeks there may be a sudden rupture of the extensor pollicis longus tendon in its osseofibrous tunnel. The pathological process involved in this complication is ischemic necrosis of the tendon, due to prolonged edema in its narrow compartment. Microscopic examination of the ruptured ends of the tendon in such cases does not reveal any evidence of granulomatous inflammation—only simple tendon necrosis. This complication is not due to one of the chronic tendon or tendon sheath diseases caused by granulomatous inflammation. However, spontaneous rupture of a tendon without significant trauma is always due to one of the granulomatous inflammations.

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THE DOGMA OF TRAUMA

Let us weigh the dogma of trauma as a cause of several common entities against the facts of granulomatous inflammation involving the extremities.

A ganglion is often the first manifestation of degenerative disease of the ligaments of the wrist, hand, ankle or foot. It usually makes a gradual appearance and pain is noticed if the area is struck; most frequently it is not noticed until some occurrence brings it to the attention of the patient. It cannot be produced by lacerating the carpal ligament, as in the wrist dislocation just described, or by surgical incision through the ligament. As a matter of fact, cure of it is effected by complete excision of the degenerated area of the carpal ligament, together with the ganglion. Here, then, significant trauma (surgical) cures a condition presumed to be caused by trauma, a paradox. Recurrence of the ganglion in the same place is due to lack of complete excision

of the degenerated portion of the carpal ligament causing the ganglion.

Taking into consideration the four moving extremities of each normal person, and the use and abuse they take in sports or work, the proportion of persons who have this disease is almost infinitesimal considering these four parts which are exposed daily to so-called microtrauma. Why perform surgical operation, a maximal trauma, if minimal trauma can cause this condition? Before surgical procedures were perfected for this condition, it was common practice to pound the ganglion with a book to rupture it.

A collection of fluid in a tendon sheath is not a ganglion. Following significant trauma, either hemorrhage or a serous effusion may occur. This condition runs a normal course of absorption, which may be aided by aspiration with a needle; it does not recur at intervals and does not become chronic. Where an effusion in the tendon sheath does persist, or recur, then the diagnosis that it was of traumatic origin becomes suspect. The pathological reason for chronic tenosynovitis with effusion is that it is one of the granulomatous inflammations, currently classified as one of the rheumatic diseases. Crepitating, or villous tenosynovitis, with or without "rice bodies" (not due to tuberculosis or to any known animate agent) is due to one of the inanimate (chemical or physical) agents, the more common ones being cholesterol, uric acid or rheumatoid factor, singly or in mixed lesions.

A granulomatous inflammation now thought to be produced by collagen (inanimate agent) is Dupuytren's contracture of the palmar or plantar fascia (also Peyroni's disease, and probably torticollis).

Dupuytren, a French surgeon, described this condition first in 1831. It affects less than 2 per cent of the adult population, and occurs chiefly in men. It is seldom seen in Negroes or in Indians. Most persons who have it are unaware of the early manifestations of this disease unless they experience an acute inflammatory attack in one or more nodules of the fascia, accompanied by tenderness and redness of the overlying skin.

Following the injury of a hand or wrist requiring a few weeks of bandaging or being in a plaster cast, the patient may suddenly discover the condition and honestly believe he never had it before because he has been unable to appreciate that it had begun insidiously several years previously. In such cases it usually can be found, in one stage or another, in the uninjured hand. It is most often bilateral and may be more advanced in one hand than the other. The major hand is not always involved to a greater extent than the opposite.[4]

Gout is a systemic disease due to an inborn inability to excrete uric acid normally. A common misconception of manifestations of gout is that it only occurs in the great toe, or that tophi can only be found in the ears. This granulomatous inflammation caused by uric acid (inanimate agent) can manifest itself in any joint and in any bursa or synovial space (as well as many other parts and organs of the body). In those afflicted with tophaceous gout, uric acid deposits are found in one or multiple locations, commonly subchondral areas adjacent to the collateral ligaments of joints, and in bursal and synovial spaces. Such a deposit in one of these areas may form a weeping sinus through the skin, which is seen most frequently in the digits but sometimes in the skin over the olecranon bursa. Gouty periarthritis may be confused with other forms of arthritis.

If an acute inflammatory episode occurs, which responds to adequate dosage of colchicine, it is certainly very likely acute gout; if the patient does not remember, or does not wish to remember, any previous attacks, it may be the first attack. Occasionally gout is associated with the granulomatous inflammation of rheumatoid arthritis, the cause of which is unknown, but recently has been associated with the rheumatoid factor (inanimate agent).

Direct significant trauma to a subcutaneous bursa usually ruptures the bursa lining and the sac fills with blood. This resolves with, or without aspiration in a short period of time and does not recur or become chronic. It can occur again after another trauma, but a new hemorrhage cannot occur spontaneously without bursting of a blood vessel. An acutely swollen bursa with warm red skin overlying it is most frequently caused by the granulomatous inflammation of uric acid, cholesterol or both, and is not due to "think back" trauma, or "must have bumped it" trauma. In bursitis of this type, microscopic studies of the lining of the bursa prove the diagnosis. Specific therapeutic treatment causes the inflammatory reaction to rapidly subside. Opacities seen in x-ray films of these areas often also are reversible by systemic medication.

Adventitious bursae can be caused by specific repeated occupational trauma (as in hod-carrying, hardwood floor laying) but these bursae do not develop granulomatous inflammations from such trauma.

This question has always been helpful when making a diagnosis: What would you, as a physician, expect would happen following a certain describable trauma; and, drawing on your experience in many similar cases, what has been the effect of this type of trauma on the part so injured?

It is doubtful if any physician would subscribe to a statement that a blow that fractured ribs over the heart could cause rheumatic endocarditis. However, there are many who will subscribe to a statement that a severe blow, or even a minor one, in the region

of a joint can cause the development of some chronic condition, whatever it may be—bursitis, epicondylitis, tenosynovitis, gouty periarthritis, rheumatoid or degenerative arthritis.

Barritt[1] said that a physician should render a medical opinion based on *reasonable medical probabilities.* (Be it noted he did not say *possibilities.*)

It takes more mental energy to think about the role of the reticuloendothelial cells, and their proliferative reaction which displaces normal cells in tissues in granulomatous inflammatory disease, than to accept common offhand epithets such as "wear-and-tear" or "microtrauma" in the etiologic description of these conditions. Forbus[3] suggested that a further understanding of the granulomatous inflammatory reaction may lead to a solution of the cause of genuine neoplasia.

There are a number of other conditions which have been blamed on trauma, among them xanthoma of tendons, which is caused by a hypercholesteremic familial metabolic disorder; spontaneous rupture of tendons in their osseofibrous tunnels from rheumatoid arthritis; peripheral median nerve neuritis due to rheumatoid, or other types of tenosynovitis of the flexor tendons in the carpal tunnel; trigger finger; DeQuervain's disease; nonosteogenic fibroma of bone; and Heberden's nodes.

Granulomatous inflammation can be produced by many agents, but not by trauma—by animate agents such as bacteria and coccidia; or by silica, fats and oils, collagen, cholesterol, uric acid, rheumatoid factor, Bence-Jones protein; or by unknown agents, as in Hodgkin's disease, rheumatic fever, mycosis fungoides, and sarcoid of Boeck.[3]

Some of the more common types of disease affecting the extremities during the years of employment are fibrositis, myositis, bursitis and so-called epicondylitis, which only affect a small proportion of the 11 million Americans afflicted with arthritis and related rheumatic diseases. Some of these conditions run a course independent of treatment, and some of the effects of the disease are reversible without treatment. Most of them have a tendency to recur at more or less frequent intervals, or to be chronic. None of the rheumatic diseases or granulomatous inflammations presented here as examples have ever been created by slight or severe mechanical trauma either in experimental animals or in human beings.

These diseases are associated with dysfunction of the reticuloendothelial system, and trauma does not produce a persistent stimulative effect on the cells of the reticuloendothelial system. The course of the granulomatous inflammations is toward chronicity and recurrence. These lesions may be reversible, may end in scarring, or may cause total progressive dissolution of tissue or total destruction of the individual.

The problem lies not so much in a lack of pathological reasoning and understanding as in specious socio-economic reasoning—almost as if when a patient says something is so, his physician must say it is so in order to keep out of an argument that may affect his economic status and thus avoid conflict with the patient, a labor union or the patient's employer. It is granted the impact of such reasoning was greater during the earlier part of the past 50 years of the age of industry, for in those days there was limited insurance coverage, particularly for off-the-job occurrences. Now, with most industrial employees covered by an umbrella of insurance both on and off duty, fewer and fewer young physicians will be exposed to this unsound concept, and it is now more likely that the physician will be remunerated for services that once would not have been paid for if the condition were certified as not being industrially connected from the standpoint of scientific fact and probability.

When a patient who attributes a disease of the extremities to on-the-job trauma is found, upon physical examination, to have one of the granulomatous diseases dealt with herein, rather than a "compensable" injury, the physician can do the patient a worthwhile service by making an accurate diagnosis and informing him of the real nature of his illness.

As Thannhauser said, "every patient is a new experience and a challenge to the keenness of our senses."[5]

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REFERENCES

1. Barritt, J. L.: Ind. Med. & Surg., p. 417, Sept. 1956.

2. Coodley, E.: Calif. Med., Vol. 88, No. 5, May 1958.

3. Forbus, W. D.: Granulomatous Inflammation, American Lecture Series, Pub. No. 1, Monograph, 1949, Charles C. Thomas, Publisher, Springfield, Ill.

4. Moorehead, J. J.: N. Y. State J. Med., Vol. 56, No. 23, Dec. 1, 1956.

5. Thannhauser, S. J.: Preface to Second Edition Lipidoses, 1950, Oxford University Press, New York.

Femoral Shaft Fractures

A Study of Closed Reduction and Open Treatment

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• **A comparative study was made of 58 cases of closed femoral shaft fractures treated by skeletal traction, and 24 cases of closed femoral shaft fractures treated by open reduction with internal fixation.**

Although complications occurred in some cases, intramedullary nailing appeared to be the most satisfactory method, resulting in primary union, in decreased time of recumbency and time in hospital, in earlier ambulation and in less residual disability.

Success of intramedullary nailing depends largely upon adequate training or experience of the surgeon in the technical operative aspects of the procedure and in postoperative management.

Placing supplemental autogenous iliac bone chips at the fracture site in closed femoral fractures in which intramedullary nailing is performed appears to enhance callus formation and bony consolidation.

Skeletal traction should be utilized on all patients whose general physical condition does not permit operative intervention.

FEMORAL SHAFT FRACTURES are severe disabling injuries that demand critical evaluation as to the method of treatment. Two generally accepted methods are being utilized in this country at present, namely, skeletal traction-suspension, and open reduction with internal fixation, especially by means of intramedullary nails. Brav and Jeffress,[1] Cave[2] and Street[7,8] have reported uniformly good results with intramedullary nailing and they hold that a more anatomical reduction, earlier ambulation, decreased hospitalization time and less residual disability are distinct advantages over other methods. McKeever[3] found that other methods did not offer particular advantages over treatment by traction-suspension, although intramedullary nailing was not included in his series.

The basis of the present report is a review of 80 patients who had closed femoral shaft fractures, some of whom were treated by skeletal traction-suspension, and the remainder by open reduction with internal fixation.

Method of Study

The 80 patients in the series were treated on the orthopedic surgical service of the Veterans Administration Hospital in Los Angeles in the period 1946-1958. In two cases the fractures were bilateral. Three patients had open reduction with internal fixation performed at other hospitals before they were transferred to the VA hospital for postoperative management. The remaining 77 patients received all their treatment here.

Adequate follow-up study was available on 66 femoral fractures. The period of observation varied from eight months to seven and a half years, averaging slightly over two years.

Only closed fractures were considered in this study, inasmuch as open fractures presented problems of wound contamination with more likelihood of infection, thus making them candidates for primary treatment by skeletal traction only, which is the policy at this hospital. No fractures resulting from disease of the bone were included in this study.

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Presented before the Section on Orthopedics at the 88th Annual Session of the California Medical Association, San Francisco, February 22 to 25, 1959.

Skeletal Traction-Suspension

Fifty-eight fractures in 56 patients were treated by traction-suspension. Skeletal traction was accomplished by the insertion of a Steinmann pin or Kirschner wire through the proximal tibia or supracondylar area. A Thomas splint and Pearson attachment were utilized for balanced suspension. Traction weight was varied according to the progress of fracture alignment, as determined by periodic roentgenograms. Traction was continued until the fracture site was thought to be clinically stable, the time varying from nine weeks to 36 weeks, averaging approximately 13 weeks. Immobilization was further continued in a plaster spica for an additional nine weeks to 30 weeks, depending upon roentgenographic evidence of solid callus formation or actual bony union.

Complications and results in the group treated by traction-suspension. There were eight instances of delayed or nonunion after 16 to 42 weeks of traction-suspension and immobilization. Eight fractures could not be reduced satisfactorily after three to five weeks of traction and attempted manipulation. One patient refractured the femur 20 weeks after the initial injury. These 17 complications required open reduc-

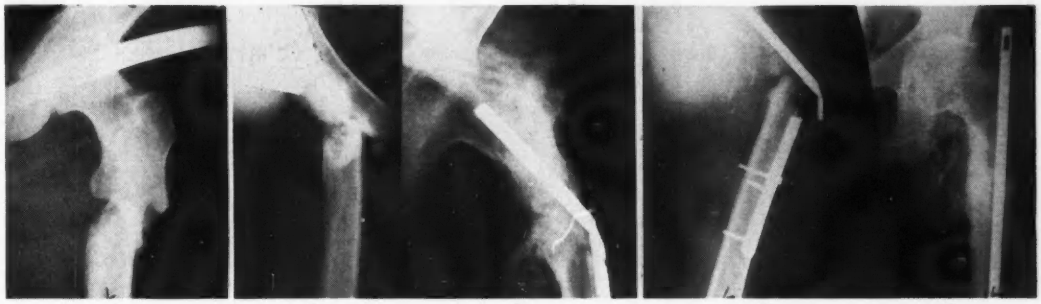


Figure 1.—*A*, high subtrochanteric fracture; *B*, nonunion after seven months of skeletal traction; *C*, eight days after blade-plate fixation and bone graft; *D*, fracture of blade-plate fixation 17 weeks after operation; *E*, solid union 14 months after intermedullary nailing and bone graft.

tion with internal fixation and bone grafting. Intramedullary nails were used in 13, blade-plate fixation in two, transfixion screws in one and plating in one.

Pin-tract infection occurred in one case, and in another severe pyodermia after prolonged immobilization in a spica cast. Conservative treatment sufficed.

Bilateral renal calculi developed in two patients, who were referred to the urological service for definitive care. Severe pyelonephritis developed in two cases and pneumonia in one. All responded satisfactorily to antibiotics.

Twenty-eight fractures healed by primary union. In 17 patients solid union was obtained after secondary open reduction and internal fixation and bone grafting. One patient in this group fractured the blade-plate fixation 16 weeks postoperatively, and subsequent intramedullary nailing and bone grafting was done, bony union eventually being obtained (Figure 1).

Knee motion was normal in 28 cases. Full extension was lacking in eight, and four patients could not flex the knee to 90 degrees. There were eight patients who could neither fully extend the knee nor flex it to 90 degrees.

Twenty-seven patients had measurable femoral shortening, 22 of them so much that shoe correction was required to prevent limping.

Twenty-eight patients were returned to full activity and had no complaint or apparent residual disability. Nineteen patients had to modify their physical activity due to residual knee difficulty or quadriceps weakness.

Primary Open Reduction and Internal Fixation

Twenty-four patients were treated by primary open reduction and internal fixation. This was done electively within four to sixteen days after the fracture had occurred.

The preoperative care consisted of (1) correction of traumatic shock and depleted blood volume by administration of whole blood and intravenous fluids; (2) skin or skeletal traction to maintain femoral length and provide comfort for the patient; (3) evaluation of other injuries if existent, and appropriate therapy as indicated.

Intramedullary nailing. Primary intramedullary nailing was performed in 19 cases. The clover-leaf nail was used in 17; in the other two, done early in the series, a large Steinmann pin and V-shaped nail were used. The nails were inserted retrograde and driven distally in the manner described by Smith[4,5] and Street.[7,8] Roentgenograms were usually made to determine the location of the distal end of the nail, and alignment at the fracture site. Additional screws or circumferential wires were used as fixation for large fragments in comminuted fractures. In three recent cases, autogenous iliac bone chips were packed around the fracture site.

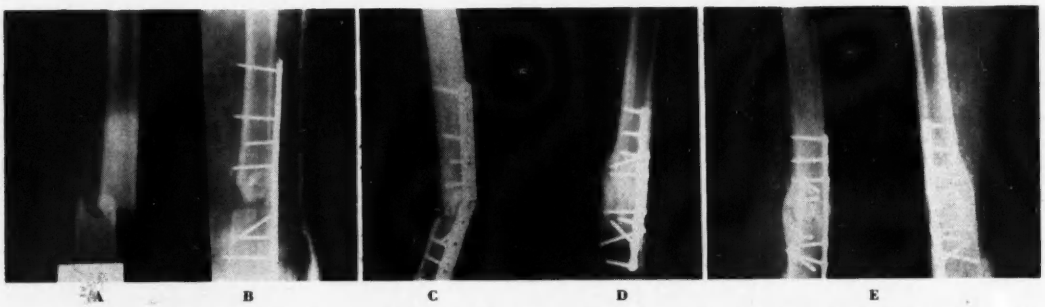
Postoperative management consisted of administration of antibiotics, elevation of the affected extremity, and balanced suspension for from eight to thirty days. Knee motion was encouraged on the first or second postoperative day. Ambulation was permitted, with partial weight bearing, in an average of four weeks following the nailing procedure. In eight cases, after there was definite evidence of bony union, the nail was removed at varying intervals of seven to 15 months postoperatively. This was done either as an elective procedure or because of pain due to nail protrusion above the trochanter.

Blade-plate or plate fixation. Four patients with high femoral shaft fractures had blade-plate fixation. A lateral approach was used, the fracture was reduced and fixation was obtained by either a Smith Peterson nail and Thornton plate, or by a Neufeld nail.

One patient with a fracture in the lower third of the femur was treated by plate fixation.

Postoperative care included bed rest or immobilization for eight to 30 weeks.

Complications and results of the group treated by



A B C D E

Figure 2.—*A*, fracture in the lower one-third of the femur; *B*, fracture fragments distracted four months after primary plating; *C*, fracture of the plate and nonunion nine months after plating; *D*, a year and a half after secondary dual plating and bone graft; *E*, three and a half years after secondary dual plating and bone graft.

A B C

Figure 3.—*A*, comminuted mid-shaft femoral fracture; *B*, showing delayed union and distraction of the fracture fragments over a 13-week period of skeletal traction; *C*, solid union 14 months after intramedullary nailing and bone graft.

primary open reduction with internal fixation. Two patients had bending of the nail, one at three weeks and the other five months postoperatively. Correction was done by manual reduction in the manner described by Soto-Hall and McCloy,[6] although in one case the nail fractured after bony union had occurred, necessitating extraction of the proximal portion later. In one case thrombophlebitis developed and was satisfactorily dealt with by anticoagulant therapy. Migration of the nail proximally occurred in one patient, necessitating reinsertion. One patient, who had been treated elsewhere, had penetration (not migration) of the nail into the knee joint. The nail was extracted after bony union was obtained. Superficial wound infection which then developed, abated under conservative treatment. Two instances of bronchopneumonia and one of pyelonephritis occurred. Treatment with antibiotics sufficed.

Two complications developed in the five patients treated by blade-plate or plate fixation. Osteomyelitis occurred in one case in which blade-plate fixation was used. The disease was quiescent for a five-month observation after removal of the metallic fixation, bone union having been obtained. In the one case in which plating was used, the plate was fractured nine months postoperatively and nonunion developed necessitating open reduction with internal fixation by dual plating and bone grafting.

Primary union was obtained in 15 cases in which intramedullary nails were used. Knee motion was normal in 14, but in one the patient could not fully extend the knee. Femoral shortening occurred in three patients, but only one of them required a shoe correction. Twelve patients were returned to full activity or were able to participate in active sporting events. Three patients had to limit their physical activity because of quadriceps weakness.

None of the group treated by blade-plate fixation had restriction of knee motion or femoral shortening, and all were returned to full activity.

In the case in which the plate used for fixation fractured, bony union was obtained after subsequent open reduction, dual plating and bone grafting, but knee motion was decidedly restricted, quadriceps strength was reduced and femoral shortening required shoe correction. The patient's physical activity was greatly restricted (Figure 2).

DISCUSSION AND COMMENT

Several factors in the statistical data in Table 1 are worthy of separate comment.

1. The period of recumbency in the group treated

Table 1.—*Data on 80 Patients with Femoral Shaft Fracture Treated Either by Closed Reduction or by Open Reduction and Nailing or Plate Fixation*

	Skeletal Traction	Intramedullary Nailing	Blade-Plate or Plating Fixation
No. of patients	56	19	5
No. of fractures	58	19	5
Age (range in years)	21-76	17-78	37-66
Average age (years)	39	38	55
Location of fracture:			
Middle one-third	40	14	0
Upper one-third	14	3	4
Lower one-third	4	2	1
Type of fracture:			
Transverse, oblique or spiral	38	11	2
Comminuted	20	8	3
Time in bed or immobilization:			
Range (weeks)	4.5-48	1.5-7.5	9-25.7
Average (weeks)	25	4	13
Time in hospital:			
Range (weeks)	4-103	4-45	14-49
Average (weeks)	26.3	12.3	29
Complications:			
Orthopedic	19	6	2
Medical or other	5	3	0
Mortality	0	0	0
Results*			
Primary bony union	28	15	3
Bony union after secondary open reduction, internal fixation and bone graft	17	0	1
Knee motion:			
Normal	28	14	3
Lack of 180 degrees of extension	8	1	0
Lack of 90 degrees of flexion	4	0	0
Lack of both 180-90 degrees of motion	8	0	1
Femoral shortening:			
None	22	12	3
1 inch or less	19	3	1
More than 1 inch	8	0	0
Disposition at last follow-up visit:			
Full activity	28	12	3
Restricted activity	19	3	1
Insufficient follow-up period	11	4	1

*12 patients were lost to adequate follow-up study and 4 patients are still under clinical observation. These 16 patients are not included in evaluation of results.

by intramedullary nailing was less than one-sixth that of the group treated by skeletal traction, and less than one-third that of the group treated by blade-plate or plate fixation.

2. The period of hospitalization of the group treated by intramedullary nailing was less than half that required by the other two groups.

3. Primary bony union was obtained in 15 of 19 patients treated by intramedullary nailing, and in three of five treated by blade-plate fixation. In the traction-suspension group of 56 patients, 28 obtained primary union.

4. The residual disability of the group treated by intramedullary nailing and blade-plate fixation was far less than that of the group treated by skeletal traction or by plating.

Delayed union or nonunion was a complication in eight patients treated by traction-suspension. Winant[10] reported a similar occurrence in 68 cases reviewed, although the majority of fractures in that group were open. The reasons for delayed or nonunion in the present series are not clearly understood, although a review of the roentgenograms made during the period of traction revealed distraction or separation of the fracture fragments in five instances (Figure 3).

The multitude of technical operative difficulties have been described by many other investigators and it is not within the scope of this report to repeat them. However, there are certain factors which appear to influence the success or failure of intramedullary nailing.

1. *Experience and training of the surgeon.* This should be obvious. The selection of patients, knowledge of the many instruments and their proper application; the technical operative difficulties which can arise and the postoperative management are

problems which can best be dealt with by surgeons who have had adequate training and experience in operative treatment of damage to bones, particularly femoral shaft fractures.

2. *Selection of the proper length and width of the nail.* The right length can be determined before operation by making scanograms on the unaffected femur or by direct measurement from the lateral femoral condyle to the top of the trochanter, depending upon the ease with which the trochanter can be palpated. As to the width of the nail, it should be the same size as the reamer, if one is used; and in unusually wide femoral canals, two Kuntscher nails can be utilized by stacking one inside the other and driving them distally.

3. *Selection of patients.* Intramedullary nailing should always be done as an elective procedure—should be used only if and when the general physical condition of the patient has been satisfactorily stabilized.

4. *Selection of fractures.* Fractures in the midshaft, in the upper one-third and in the upper portion of the lower one-third are amenable to intramedullary nailing.

The addition of autogenous iliac bone chips around the fracture site, as recommended by Brav and Jeffress[1] and Thomson,[9] appears to enhance earlier callus formation and bony consolidation.

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REFERENCES

1. Brav, E. A., and Jeffress, V. H.: Fractures of the femoral shaft; a clinical comparison of treatment by traction suspension and intramedullary nailing, Am. J. Surg., 84:16, 1952.

2. Cave, E. F.: Femoral shaft fractures treated by medullary nailing, N.E.J.M., 246:284, 1952.

3. McKeever, F. M.: Fracture of the shaft of the femur in adults; evaluation of methods of treatment, J.A.M.A., 128: 1006, 1945.

4. Smith, H.: Medullary fixation of the femur, Radiology, 61:194, 1953.

5. Smith, H. (Ed.): Symposium on Medullary Fixation. American Acad. Ortho. Surgeons, Instructional Course Lectures, 8:1, Ann. Arbor, 1951, J. W. Edwards.

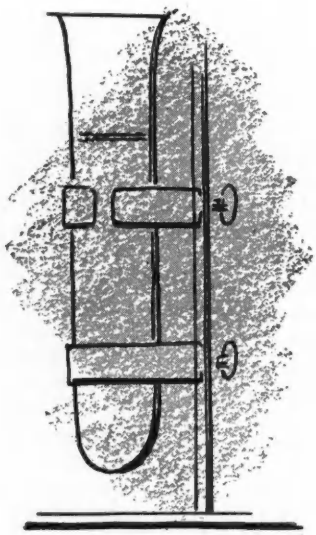
6. Soto-Hall, R., and McCloy, N. P.: Cause and Treatment of Angulation of Femoral Intramedullary Nails, Clin. Orth. 2:66, Philadelphia, 1953. J. B. Lippincott Co.

7. Street, D. M.: 100 fractures of the femur treated by means of a diamond-shaped medullary nail, J.B.J.S., 33A: 659, 1951.

8. Street, D. M.: Medullary nailing of the femur: Comparative study of skeletal traction, dual plating and medullary nailing, J.A.M.A., 143:709, 1950.

9. Thomson, J. E. M.: Non-Union and Mal-Union of Fractures of the Lower Extremity Treated by Medullary Fixation. Clin. Orth. 2:142, Philadelphia, 1953. J. B. Lippincott Co.

10. Winant, E. M.: The use of skeletal traction in the treatment of fractures of the femur, J.B.J.S., 31A:87, 1949.



Intranasal Injection of Corticosteroids

MARVIN W. SIMMONS, *M.D.*, Fresno

• **Intranasal injections into the inferior turbinates of a slightly soluble form of prednisolone TBA (Hydeltra® TBA) into persons with complaint of nasal obstruction gave considerable relief in 78 per cent of cases. Nasal hyperfunction due to seasonal allergic rhinitis, vasomotor rhinitis and secondary nasal edema from sinusitis was the indication for use. No local or general reactions other than a small amount of bleeding at the time of injection was noted. This method allows full utilization of the anti-inflammatory activity of corticosteroids at the local tissue level without producing a systemic effect.**

A DECADE has passed since recognition was first given to changes in the mucosa of the upper air passages under stimulation of the pituitary adrenocorticotropin hormones and the adrenal corticosteroids.[5,18] Following reports of Bordley and his co-workers,[2,3,4] many authors indicated relief of symptoms of allergic diseases with administration of these hormones parenterally and orally.[9,10,17] The severest forms of nasal allergic reaction and bronchial asthma often subsided completely. Swelling of affected nasal mucous membranes subsided, a more normal pink color returned and the thick gelatinous mucus characteristic of allergic reaction disappeared. The nasal turbinates became smaller and the air space became larger. Nasal polyps lost their translucence, began to shrink and in many instances disappeared.

Later topical use of corticosteroids by nasal sprays was reported to avert many systemic side effects. An early report in 1951 by Dill and Bolstead[6] indicated that cortisone nasal spray produced a more or less temporary effect. Objectively, the use of the solution lessened nasal secretions and decreased edema of the nasal mucosa. They noted too, that many patients had relief of mild asthmatic symptoms such as wheezing, cough and tightness of the chest. Also headache of allergic origin was relieved and polyps shrank. They noted no untoward effects and no atrophy of nasal mucosa. Subsequently, in 1952 Dill and Bolstead[7] stated that only half their patients had some relief of allergic symptoms from cortisone sprays and only while using the spray.

Williams[20] in 1952 observed that results of giving cortisone by mouth for reduction of nasal polyposis were disappointing. Other medical and surgical measures gave more lasting results, he believed.

Semenov[13] described injections of cortisone directly into nasal polyps. One patient a minute or two after the injection had weakness, dyspnea, substernal pressure, flush of the entire face, wheezing, rapid, weak pulse and collapse. All these symptoms disappeared within an hour. In a later discussion[8] Semenov said that hydrocortisone is twice as potent and more effective topically than cortisone. He stated he had injected 5 mg. of Cortone® acetate into the nasal mucosa hundreds of times without mishap, whereas a dose of 25 mg. evoked severe reactions in three patients.

In 1952 a very favorable report was issued by Wall and Shure[19] after intranasal injection of cortisone in 52 patients with unmistakable allergic rhinitis; 42 had pronounced improvement. In all cases of acute allergic rhinitis, results were excellent, they said. They also reported two severe, immediate, unexplainable constitutional reactions which left no after-effects. At the conclusion of their report they advocated the intranasal injection of cortisone into the inferior turbinates for prolonged symptomatic relief of allergic rhinitis, especially of the acute seasonal variety.

Multiple studies using cortisone as packs and drops in allergic rhinitis followed. Evans[8] in 1954 recommended continuous and more widespread use of these methods by the medical profession.

Grace, in discussing Evans' paper, stated he had used cortisone topically "without any startling results." However, he said that injections of cortisone into the nasal mucosa gave "splendid" results. The dosage he used was 2.5 mg. in a series of four injections and no bad reactions occurred.

In 1954 Smith[16] used hydrocortisone in a nasal jelly in allergic rhinitis, together with specific hyposensitization. He reported topical therapy more effective than submucosal injection into the nasal turbinates in relieving symptoms.

In 1955, Sidi and Tardif[14] reported on intranasal injections of hydrocortisone acetate (compound F) into the anterior third of the inferior turbinates of the nose for treatment of allergic rhinitis. They noted favorable results in 30 of 50 cases. Two of the 50 patients complained of a sensation of thoracic constriction after the injection followed by pain in the lumbar region. This reaction did not last more

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than four minutes. The dosage these investigators used was never more than 6 mg. of hydrocortisone acetate at one time.

All patients with allergic rhinitis treated by Anderson and Ogden[1] were helped by nasal sprays of prednisolone. These investigators said that pharmaceutically prednisolone is considered several times more potent than hydrocortisone.

In 1958 Myers[11] reported on the treatment of allergic nasal polyps by intrapolyp injection of prednisolone TBA.* He noted no untoward reactions and said that results were excellent.

Doses of about 30 to 40 mg. were employed at each treatment.

MECHANISM OF ACTION

Several properties of the corticosteroids may explain why they are effective in nasal disease. The human organism attempts to maintain homeostasis through the pituitary-adrenal axis hormonal secretions. Allergic reaction may well be due to inability of the organism to either produce sufficient, effective cortical hormones or inability of specific shock organs to utilize them. Why many patients respond poorly to stress—whether due to allergy, infection or emotions—may be explained on the basis of inadequate function of the pituitary-adrenal axis.

Nasal inflammation and hyperfunction is produced in susceptible persons by any stress whether due to allergy, infection or emotions. Edema is primary in this inflammation and believed located in the gel of connective tissue. The enzyme hyaluronidase present in connective tissue is liberated. In inflammation the enzyme liquefies the gel with resultant edema. Hyaluronidase also disrupts the integrity of the capillary endothelial cell, increasing capillary permeability and enhancing edema. The corticoids are believed to neutralize hyaluronidase, hence controlling the inflammatory edema. A good deal of evidence that large doses of the corticoids lower resistance to infection but small doses increase resistance,[12,15] has accumulated. Acute infectious rhinitis appears to improve with small doses of corticoids.

In other words, these hormones help keep a good peripheral vascular bed, improve smooth muscle tone, maintain a healthy capillary endothelium and preserve the ground substance of connective tissue. Since corticosteroids are effective in all inflammatory disorders, steroid injections need not be confined to allergic nasal disease. In many cases, it is impossible to make specific delineation between nasal allergic disease and infectious rhinitis or nasal changes from emotions or weather changes. Finding eosinophils in the nasal smear is not pathognomonic of nasal allergic disease. Wolfe[21] showed that eosinophilia locally and in the peripheral blood occurs with nasal hyperfunction associated with emotional stress. He also observed that polymorphonuclear leukocytes occurred with the eosinophils in emotional stress with no apparent allergic reaction or infection. Wolfe demonstrated that the nose reacts similarly in any disease that affects that organ—namely, with hyperemia, nasal obstruction, turbinal and mucosa swelling and increased secretions. Sneezing may occur. This reaction represents a defense to shut off from the organism what is harmful or unpleasant whether it is a viral, bacterial, pollen or a disagreeable emotional reaction. Color changes of the nasal mucosa from pale violet to scarlet may give a clue as to whether allergic disease or infection predominates. But, here again specificity is absent.

The effectiveness of the pituitary-adrenal axis theoretically determines the extent of the reaction and the speed to which normal conditions return. Seemingly, local injection of the corticosteroids, especially in a transitory episode, should hasten return to normal function of the nose. In addition, increased concentration of the hormone in the tissues may act as protection against assault by pollen, bacteria or emotional stress.

INDICATIONS

The indication for the use of intranasal prednisolone is primarily the relief of nasal obstruction caused by edema of the inferior turbinates. Vasomotor rhinitis is a generic term reserved for this condition. Edema may occur in seasonal allergic rhinitis, in infection as in bacterial rhinitis secondary to infectious sinusitis, and in emotional reactions as described by Wolfe.[21] Acute nasal edema as in coryza lasts but a few days and is self-limited. Intranasal injections of prednisolone are recommended for longstanding and recurrent nasal edema recalcitrant to other therapy. No contraindications exist.

PRESENT STUDY

The basis of this report is the use of a series of three nasal turbinate injections of corticosteroids in the treatment of 419 patients with vasomotor rhinitis of various causes. There were no side reactions of importance. Some psychological anxiety existed with the mention of a needle. When the patient realized that the procedure is painless no further apprehension was apparent. A slight amount of cocaine solution may be sprayed on the anterior ends of the inferior turbinates before injection. A small amount of bleeding occurs at the time of each injection, especially if considerable congestion exists. The bleeding ceases within a few minutes. Although clinically

*In the form of suspension Hydeltra® TBA—Produced by Sharp & Dohme, Division of Merck & Co.

successful results were obtained with cortisone and hydrocortisone, my impression was that Hydeltra® TBA* (prednisolone) was so much more effective that the use of the other corticosteroids was soon discontinued. Hydeltra® TBA, a very slightly soluble ester of prednisolone, is capable of producing a longer and more pronounced local anti-inflammatory effect when injected than does hydrocortisone or cortisone. The manufacturers state that, since Hydeltra® TBA is so very slightly soluble, 18 to 24 hours may elapse following injection before there is a change in its chemical structure with subsequent absorption in local tissues and effective relief of symptoms. My experience agrees with that claim.

Initially, 0.2 cc. (8.0 mg.) was injected into each anterior end of the inferior turbinate as superficially as possible. This was repeated usually in three to four days, and again about a week after the second injection. The patients usually had relief for varying periods up to a year or more. If the patient returned with a recurrence of symptoms, larger doses appeared necessary at the second series to give the same relief—0.3 cc. (12 mg.) Hydeltra® TBA for each turbinate at each treatment.

During the year 1958 questionnaires were mailed to 419 individuals who had received a series of three injections for various nasal complaints, the last injection more than one year previous. Of this number, 195 returned the questionnaire. Reporting only their own subjective observation, 152 (78 per cent) stated that they had had considerable relief of their nasal complaints for at least six months, 67 (44 per cent) saying they had had no return of their symptoms for at least one year. Many had had complete relief since the time of therapy for as long as three years.

Of the 419 persons who received the series of three injections, 298 (71 per cent) had typical histories of seasonal allergic rhinitis. Vasomotor rhinitis was the diagnosis in 109 patients (26 per cent) who complained of perennial nasal obstruction. The cause was uncertain but the majority admitted being tense and anxious. Allergic sensitivity is difficult to prove in this group. Sinusitis resulting in secondary nasal edema was confirmed in 12 patients (3 per cent).

A diagnosis of allergic seasonal rhinitis had been made in 110 (72 per cent) of 152 patients who stated in the questionnaires that they had had relief of symptoms. The remaining 42 (28 per cent) had long-standing vasomotor rhinitis of uncertain cause.

Several days following an injection, the nasal mucosa, whether pale blue or violet from allergic reaction or bright red or pink from infection, returns to a normal pink color. A noticeable subsidence of edema becomes evident, with pronounced decrease of secretions. At the end of the third injection, oftentimes, the turbinal bodies appeared fibrous. Cardinal relief noted by the patients was ease in breathing and lack of a feeling of obstruction. Many also commented on the disappearance of postnasal drip and regaining a sense of smell. Sometimes one injection of prednisolone relieved the symptoms when the obstruction had been present for a number of days to several weeks. The symptoms did not recur.

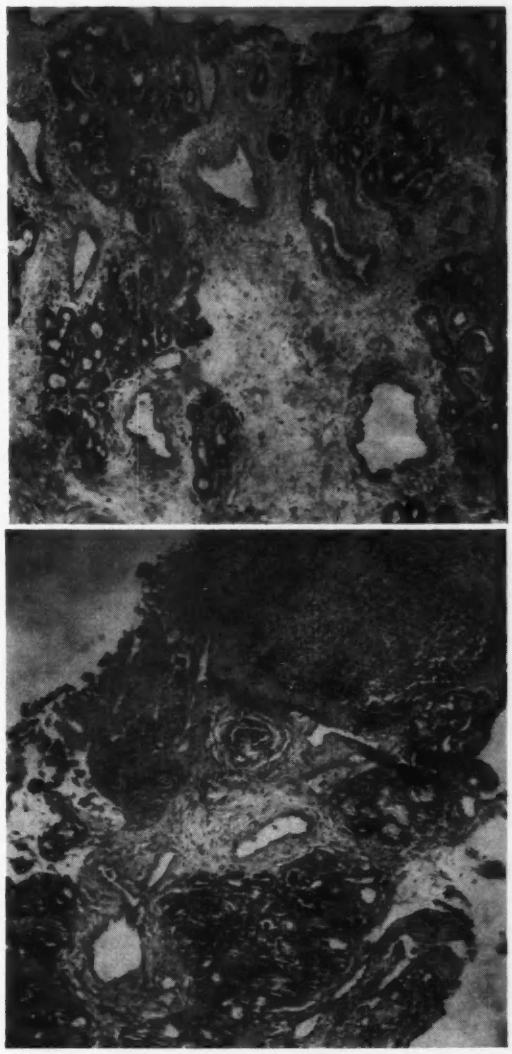

Figure 1.—*Above:* Section of inferior turbinate of individual complaining of nasal obstruction. Note marked edema, engorged blood spaces and increased thickness of the connective tissue layer. *Below:* Section of same inferior turbinate one month later following three injections of prednisolone. Edema has subsided, the blood spaces are smaller and the connective tissue layer is reduced considerably. (×100)

*Supplied by Sharp & Dohme, Division of Merck & Co.

In biopsy of tissue taken from the inferior nasal turbinates in some cases, no pronounced microscopic changes were noted aside from decrease in edema of the tissue. The amount of connective tissue present was neither greater nor less than normal, nor was there any evidence of the injected material within the tissues. (See Figure 1.)

Direct injection of Hydeltra® TBA into polyps was disappointing. Some shrinkage was noted but never complete disappearance. Surgical removal of large polyps was always necessary. I believe that prednisolone injections offer an expediency in relieving transitory nasal hyperfunction regardless of the etiologic factor, whether allergic sensitivity, infection or emotional disturbance. They are also a help sometimes in chronic nasal disease if irreversible changes have not already taken place.

Time-tested methods of pollen desensitization and surgical operation on the nasal septum and on polyps are still in order when indicated. Sinus disease may be a result of nasal dysfunction or complicated by it. The principles of drainage and ventilation may require very conservative sinus operations, but seldom are such procedures indicated. Hydeltra® TBA intranasal injections will promote drainage and ventilation of the sinuses by decreasing nasal edema.

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REFERENCES

1. Anderson, J. R., and Ogden, H. D.: Topical use of prednisolone in nasal allergies, Ann. of Allergy, 14:44, Jan.-Feb. 1956.

2. Bordley, J. E., Carey, R. A., Harvey, A. M., Howard, J. E., Katus, A. A., Newman, E. V., and Winkenwerder, W. L.: The preliminary observations in the effect of adrenocorticotropic hormone (ACTH) in allergic diseases, Bull. Johns Hopkins Hospital, 85:396-398, 1949.

3. Bordley, J. E.: Observations on changes taking place in the upper respiratory tract of patients under ACTH and cortisone therapy, Bull. Johns Hopkins Hospital, 87:415-424, 1950.

4. Bordley, J. E.: The effect of ACTH and cortisone on the upper respiratory tract, N. Y. St. J. Med., 51:2635-2639, 1951.

5. Crowe, S. J.: Otolaryngology—1940-1950. Year Book of EENT, Year Book Publishers, Inc., Chicago, 1950, pp. 237-245.

6. Dill, J. L., and Bolstead, D. S.: Observations on the local use of cortisone in the nose in allergic rhinitis, Laryngoscope, 61:415-422, May 1951.

7. Dill, J. L., and Bolstead, D. S.: Further observations on the local use of cortisone in the nose in allergic rhinitis, Trans. Acad. Ophth. and Otol., 56:214-219, March-April 1952.

8. Evans, W. H.: The use of a suspension of cortogen acetate with chlortrimeton in the treatment of allergic rhinitis of pollen origin, Trans. Amer. Acad. of Ophth. & Otol., 58: 89-103, Jan.-Feb. 1954.

9. Hotchkis, W. T.: Influence of prednisolone on nasal polyposis with anosmia, Arch. Otol., 64:478, Dec. 1956.

10. Koelsche, G. A., Maytum, C. K., Prickman, L. E., and Carryer, H. M.: Use of cortisone and ACTH in the management of nasal allergy, Ann. of Allergy, 9:573, Sept.-Oct. 1951.

11. Myers, D.: Experiences in the treatment of the allergic nasal polyp by the intrapolyp injection of prednisolone T.B.A., Laryngoscope, 58:1-17, Jan. 1958.

12. Rawlins, A. G.: Otolaryngologic aspects of the corticosteroids, Trans. Amer. Acad. of Ophth. & Otol., 60:509-518, July.-Aug. 1956.

13. Semenov, H.: The pathology of the nose and paranasal sinuses in relation to allergy, Tr. Am. Acad. Ophth. & Otol., 56:121-170, March-April 1952.

14. Sidi, E., and Tardif, R.: Treatment of allergic rhinitis associated with eczema with hydrocortisone acetate injected into nasal mucous membranes, Semaine des Hosp. de Paris, 35:1922, May 30, 1955.

15. Silcox, L. E.: The intranasal use of hydrocortisone alcohol, A.M.A. Arch. Otol., 60:431-439, Oct. 1954.

16. Smith, T. T.: Local use of hydrocortisone acetate in the nose, A.M.A. Arch. Otol., 60:24-36, July 1954.

17. Stewart, J. P., and Kawa, M. Z.: Further observations on the effect of cortisone and ACTH in the treatment of allergic rhinitis, J. of Laryng. & Otol., 68:193, April 1954.

18. Thorn, G. W., Boyles, C. B., Massel, B. F., Forsham, P. H., Hill, S. R., Smith, S., and Warren, J. E.: Studies in the relation of pituitary adrenal function to rheumatic disease, N.E.J.M., 241:529, 1949.

19. Wall, J. W., and Shure, N.: Intranasal cortisone; preliminary study, A.M.A. Arch. Otol., 56:172-176, Aug. 1952.

20. Williams, H. L.: Use of cortisone and corticotropin in the field of otorhinology and laryngology, Ann. Otol., Rhin. & Laryng., 61:497-504, June 1952.

21. Wolfe, S. G., Jr.: Causes and mechanisms in rhinitis, Laryngoscope, 62:601-614, June 1952.

Cardiac Arrest

Successful Resuscitation in the Hospital Outside the Operating Rooms

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• **It is believed that if physicians generally can bring themselves to carry out the drastic action necessary, the benefits of cardiac massage for patients with reflex inhibition of heartbeat can be extended to most cases of this kind occurring anywhere in a hospital, even though there is not time to summon a surgeon or anesthesiologist.**

This concept requires that attending physicians be prepared to recognize and treat cardiac arrest in salvageable patients. To carry out massage of the heart, a short incision must be made beneath the left breast to permit grasping the heart and starting it again. Mouth-to-mouth breathing until a mask and oxygen arrive is a necessary part of the procedure.

Whether to attempt massage must be a decision entirely up to the physician on his appraisal of the circumstances; but the procedure is probably not advisable outside a hospital.

THIS ARTICLE is written to encourage physicians generally to prepare themselves intellectually, emotionally and technically to perform cardiac massage in the hospital whenever necessary to revive a salvageable patient. In the past[1,21,23,24] only surgeons and anesthesiologists were particularly concerned with this problem.

Recent hospital surveys[25] indicate that reflex inhibition of the heartbeat with cardiac arrest occurs as frequently outside the operating rooms as within. Hence, unless the physician in attendance at the time is able then and there to initiate cardiac massage himself, it is unlikely that it can be done soon enough. Summoning someone probably would take too much time. Even physicians who have performed the procedure in the operating room where everything is available to accomplish it know that it is difficult to act quickly enough, especially with one's first experience with this disaster. Even Lahey,[12] who has had considerable experience with cardiac arrest, wrote of how difficult it is for the surgeon and others participating in the procedure to function without panic and loss of time.

Although it would seem almost impossible for a physician not used to doing surgical operations to suddenly take over the role, that very thing has been done, as verified by several of the successful resuscitations recorded in this paper (Table 1). The first case, reported by Bloomfield and Mannick,[4] was that of a 41-year-old truck driver who was brought to the hospital by ambulance in shock with precordial and arm pain. Electrocardiograms showed evidence of anterior myocardial infarction. While receiving supportive measures the patient suddenly became unconscious and cyanotic without pulse or blood pressure. Pounding on his chest and needling the heart brought no response, whereupon the chest was opened by the resident internist through a 10 cm. incision beneath the left breast and massage was begun. A minute later the patient became semiconscious and asked, "What's going on?" He was asked to cooperate, which he did, saying, "Okay, Doc, anything you say." Although he required anesthesia and a long period of massage and supportive measures and finally defibrillation, he did make a satisfactory recovery and was discharged from the hospital fully ambulatory.

Perhaps initiation of massage will not be possible for many physicians at present, but progress in this direction is being made and should be encouraged. Medical schools are now including instruction in the principles and practice of cardiac resuscitation. Interns and residents in general practice and the specialties are being given instruction in this important emergency procedure. Several postgraduate courses[3] are providing training and experience with animals, which, it should be said, is the best way to learn how to proceed. Therefore, the time is not far off when physicians generally will be prepared to initiate massage when cardiac arrest occurs in the hospital, just as they now do tracheotomy when immediate action is required. Although this trend should be fostered, the final decision for or against instituting cardiac massage must be that of the attending physician and must depend upon his judgment at the time. Any pressure either legal or otherwise would result in more harm than good.

Causes of Cardiac Arrest

The primary cause of cardiac arrest elsewhere than in operating rooms appears to be a reflex inhibition of the heartbeat. The exact mechanism is poorly understood. Vagal stimulation produces bra-

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dycardia, the end point of which may be arrest, the so-called vaso-vagal reflex.[5,20,27] The contributing causes of anoxia—increased carbon dioxide, alteration of the pH of the blood[15] and the introduction of a toxic substance into the blood—may or may not be present. Panic or great fear may be a part of the mechanism. Many of the patients in whom arrest occurs outside the operating rooms are healthy persons undergoing diagnostic studies. This makes recognition and treatment even more important.

The accompanying disease or indication for hospital admission in patients successfully resuscitated is indicated in Table 1. Some of the patients were undergoing roentgenologic studies of the bronchial tree and other x-ray diagnostic procedures; others had been admitted to the emergency ward with asthma or following accidents, especially with thoracic injuries; and there were also obstetrical patients, newborn babies, patients undergoing urologic, neurologic or cardiovascular studies, and patients with cardiac disease and minor coronary occlusions. Table 1 also shows where in the hospital the cardiac

TABLE 1.—*Data on 19 Cases of Successful Cardiac Resuscitation Outside the Operating Room (Collected from the Literature)*

Author	Location	Diagnosis	Age of Patient	Physician Initiating Massage	Defibrillation	Mouth to Mouth Breathing	Duration of Massage	Adjunctive Therapy and Result
Southworth, et al.[22]	X-ray Dept.	Heart disease	25	Surgeon	Electric shock, 7	No	45 min.	Respirator; good
Turk and Glenn[25]	Patient's room	Mitral stenosis	37					Good
	Patient's room	Mitral stenosis	48					Good
	Constant temp. room	Causalgia	55					Good
Beck, et al.[2]	Hallway	Myocardial infarction	65	Surgeon	Electric shock, 5	No	25 min.	Cedilanid intravenously; oxygen; good
Celio[8]	Patient's room	Myocardial infarction	46	Surgeon			30 min.	Thorazine; good
Mozen, et al.[16]	Patient's room	Heart disease	51	Resident (surgeon)	Electric shock, 1	Yes 15 min.	27 min.	Tracheotomy; vasopressor drugs; good
Reagan, et al.[17]	Emergency room	Coronary occlusion probable	55	Surgeon	Electric shock, 3	No	18 min.	Coronary regimen; good
Brown, et al.[6]	X-ray Dept.	Not known. Vaso-vagal reflex?	24	Surgeon	Drugs only	No	2.5 hr.	O_2 intermittent, 7 days, blood, digitalis; good
Galos and Surks[9]	Delivery room	Ruptured uterus	Newborn	Obstetrician	No	No	12 min.	Thorazine, 7 days; good
Bloomfield and Mannick[4]	Emergency room	Myocardial infarction	41	Resident (medical)	Electric shock, 1	No	45 min.	Oxygen; good
	Emergency room	Myocardial infarction	50	Resident (surgeon)	Electric shock		2 hr. (intermittent)	Left sided hemiparesis
Kent[11]	X-ray Dept.	Bronchogram doubtful	32	Surgeon	Adrenalin	No	?	Hypothermia; good
McBurney[13]	Delivery room	Unknown	20	Obstetrician	Procaine	No	25 min.	Good
Schwartz and Lobell[19]	Patient's room	Rheumatic fever	54	Resident (surgeon)	Electric shock	Yes 10 min.	20 min.	Norepinephrine, 15 hrs.; pulmonary edema, 3 days P.O.; good
Williams and Spencer[26]	Emergency room	Bronchial asthma	9	Surgeon		No	5 min.	Hypothermia; good
	Emergency room	Knife wound, chest	38	Surgeon		No	5 min.	Hypothermia; good
	Emergency room	Stab wound, chest	39	Surgeon		No	5 min.	Hypothermia; good
McGregor and Newton[14]	Ward	Myocardial infarction	51	Internist	Electric shock, 2	No	29 min. 2 min.	Intravenous procanamide; good

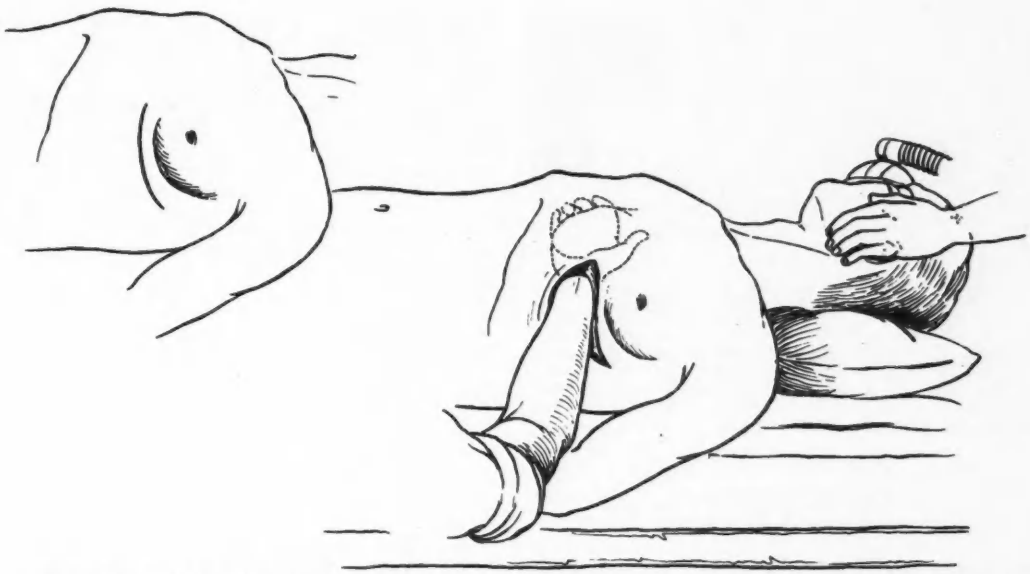

Figure 1.—A 5-inch incision has been made beneath the left breast, as indicated in the inset. With the chest thus opened, as shown in the main drawing, the hand has been forced between the ribs and the heart grasped in the cupped hand. The short incision helps to control pneumothorax. If inhalation oxygen is not available, mouth-to-mouth breathing, as illustrated in Figure 2, is carried out.

arrest occurred, to emphasize the fact that physicians present or attending the patient at the time action is needed may not be practicing general or thoracic surgery.

Recognition of Cardiac Arrest

Sudden cessation of the heartbeat in a conscious patient causes unconsciousness immediately. There is no pulse, blood pressure or heart sounds—which differentiates cardiac arrest from syncope. Respirations lag and soon cease, cyanosis usually appears, the pupils are dilated and the patient is limp. A thump over the sternum causes no response. If the heart is needled or if epinephrine is immediately available and injected into the heart and there is no response, surely the patient must die unless cardiac massage is started immediately.

Decision for or Against Cardiac Massage

If, in the hospital, cardiac arrest has occurred in a salvageable patient, if the time the heart has actually been arrested is less than four minutes, if the physician in attendance is equipped to perform the procedure (he alone can decide), and if assistance and equipment are readily available to complete the resuscitation successfully, then the attending physician should proceed with massage. There should be reasonable prospect of successful issue. It would seem that, other criteria being met, there should be no doubt as to the advisability of the procedure for a young healthy person undergoing a diagnostic study when sudden inhibition of heartbeat occurs.

Technique

The technique to be described differs slightly from that usually used in the operating room and is designed for use elsewhere in the hospital and without immediate access to equipment other than a knife. Almost all the details are indicated in Figure 1. The clothing is stripped from the patient's chest. Antiseptic preparation of the skin must be foregone. Rolling up the physician's sleeves is necessary, but obtaining and donning gloves probably would take too much time. An incision about five inches long, just big enough to admit the hand, is made beneath the left breast. A short incision will make for difficulty in forcing the ribs apart, but it facilitates control of pneumothorax if ventilation is not completely adequate. The incision is carried between the ribs through the intercostal muscles and through the pleura. The right hand is then forced through the opening and the heart is grasped as it lies in the midline beneath the sternum. It is compressed at a normal rate between the fingers and the thenar eminence of the thumb of the cupped hand. Considerable force is necessary. Unless the heart starts to beat immediately, it is necessary to force blood out through the ventricles so that a sufficient pulse can be obtained in the carotids or femoral arteries.

Simultaneously with the institution of cardiac massage, the lungs must be ventilated with oxygen. If this is not immediately available with a mask and tank, it should be supplied by mouth-to-mouth breathing (Figure 2). This is much to be preferred,

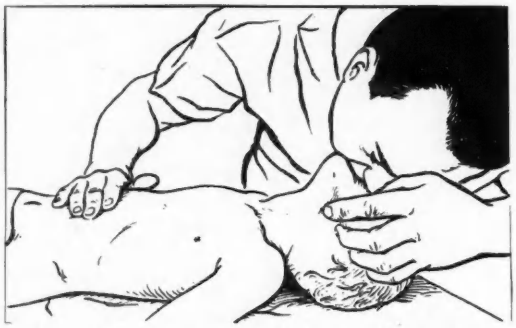

Figure 2.—With the jaw held forward with the operator's left hand, air is forced through the mouth and nose of the victim by intermittent expiration. The right hand is placed over the epigastrium to keep the stomach from filling with air.

as was observed by Gordon and coworkers,[5,10] over manipulative artificial respiration procedures both in the child and the adult, for it actually inflates the alveoli with a 16 per cent oxygen mixture which is more than adequate. To carry out the procedure, the jaw of the patient is lifted forward and the physician puffs air from his own lungs into the mouth of the patient. Expansion and recoil of the chest is then produced at about 20 times a minute until an oxygen mask or intratracheal tube arrives. A hand is pressed down on the abdomen to keep the stomach from becoming inflated.

Further details in opening the chest for better exposure, the use of epinephrine, calcium chloride,[18] the defibrillator,[1] the pacemaker,[7,28] vasopressor drugs, transfusion and fluids, hypothermia in selected patients,[14] chest closure and water-seal drainage can be utilized as indicated when a specialist arrives.

This article is written for those who would initiate the resuscitation. No detailed knowledge, experience or special information can possibly help a person in whom brain cells have been destroyed by too long an interval of cardiac arrest before institution of the simple technique here described.

It is believed that only in the hospital can cardiac massage for cardiac arrest be successfully completed except in the most unusual circumstances and, therefore, it is not advised except within the hospital.

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REFERENCES

1. Beck, C. S., Pritchard, W. H., and Feil, H. S.: Ventricular fibrillation of long duration abolished by electric shock, J.A.M.A., 135:985, 1947.

2. Beck, C. S., Meckesser, E. C., and Barry, F. M.: Fatal heart attack and successful defibrillation. New concepts in coronary artery disease, J.A.M.A., 161:434, 1956.

3. Berne, C. J., Denson, J. S., and Mikkelsen, W. P.: Cardiac arrest—problems in its control, Amer. J. Surg., 90:189, 1955.

4. Bloomfield, D. L., and Mannick, J. A.: Successful resuscitation in acute myocardial infarction with ventricular fibrillation, New Eng. Jour. Med., 258:1244, 1958.

5. Brodie, T. N., and Russell, A. E.: On reflex cardiac inhibition, J. Physiol., 26:92, 1900.

6. Brown, C. D., Knudson, J., and Schroeder, G. F.: Cardiac arrest at work—penknife thoracotomy with recovery, J.A.M.A., 163:352, 1957.

7. Callaghan, J. C., and Bigelow, W. G.: An electrical artificial pacemaker for standstill of the heart, Ann. Surg., 134:8, 1951.

8. Celio, A.: Cardiac arrest associated with coronary occlusion: Successful resuscitation, J. Internat. Coll. Surgeons, 25:299, 1956.

9. Galos, G., and Surks, S. N.: Cardiorespiratory arrest in the newborn treated by cardiac message, Amer. J. Ob. and Gyn., 74:1108, 1957.

10. Gordon, A. S., Frye, C. W., Gittelson, L., Sadove, M. S., and Beattie, E. J., Jr.: Mouth to mouth versus manual artificial respiration for children and adults, J.A.M.A., 167:320, 1958.

11. Kent, E. M.: Discussant of Reference No. 6.

12. Lahey, F. H., and Ruzicka, E. R.: Experiences with cardiac arrest, S. G. and O., 90:108, 1950.

13. McBurney, R. D.: Cardiac arrest: a case report, West. J. Surg., Obst. and Gynec., 66:150, 1958.

14. McGregor, J. G., and Newton, D. E.: The treatment of cardiac arrest following myocardial infarction, U. S. Armed Forces Med. J., 10:125, 1959.

15. Miller, F. A., Brown, E. B., Buckley, J. J., Van Bergen, F. H., and Varco, R. L.: Respiratory acidosis; its relationship to cardiac function and other physiologic mechanisms, Surgery, 32:171, 1952.

16. Mozen, H. E., Katzman, R., and Martin, J. W.: Successful defibrillation of the heart. Resuscitative procedure started on medical ward and completed in operating room, J.A.M.A., 162:111, 1956.

17. Reagan, L. B., Young, K. R., and Nicholson, J. W.: Ventricular defibrillation in a patient with probable acute coronary occlusion, Surgery, 39:482, 1956.

18. Rothberger, C. J., and Winterberg, H.: Uber die experimentelle Erzeugung extrasystolischer ventrikularer Tachykardie durch Accellransreizung: Ein Beitrag zur Herzwirkung von Baryum und Calcium, Arch. ges Physiol., 142:461, 1911.

19. Schwartz, A. M., and Lobell, S. M.: Cardiac arrest; successful treatment in a patient's room, J.A.M.A., 166:488, 1958.

20. Sloan, H. E.: The vagus nerve in cardiac arrest, S. G. and O., 91:257, 1950.

21. Snyder, W. H., Jr., Snyder, M. H., and Chaffin, L.: Cardiac arrest in infants and children, Arch. Surg., 66:714, 1953.

22. Southworth, J. R., McKusick, V. A., Pierce, E. C., II, and Rawson, F. L., Jr.: Ventricular fibrillation precipitated by cardiac catheterization, J.A.M.A., 143:717, 1950.

23. Starling, E. A., and Lane, W. A.: Report of Society of Anesthetists, Lancet, 2:1397, 1902.

24. Stephenson, H. E., Reid, L. C., and Hinton, J. W.: Some common denominators in 1,200 cases of cardiac arrest, Ann. Surg., 137:731, 1953.

25. Turk, L. N., and Glenn, W. W. L.: Results of attempted cardiac resuscitation in 42 cases, New Eng. J. Med., 251:795, 1954.

26. Williams, G. R., and Spencer, F. C.: The clinical use of hypothermia following cardiac arrest, Ann. Surg., 148: 462, 1958.

27. Young, W. G., Jr., Sealy, W. C., Harris, J. S., and Botwin, A.: The effects of hypercapnia and hypoxia on the response of the heart to vagal stimulation, S. G. and O., 93:51, 1951.

28. Zoll, P. M., Linenthal, A. J., and Norman, L. R.: Treatment of Stokes-Adams disease by external electrical stimulation of heart, Circulation, 9:482, 1954.

CASE REPORTS

Ruptured Abdominal Aneurysm with Pain in the Testicle

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THE MOST predominant symptom of ruptured aneurysm of the abdominal aorta is severe sudden pain in the lower abdomen or lower back. Pallor, the state of shock and tenderness in the abdomen or flanks are the most frequent physical findings, and sometimes a palpable abdominal mass, often pulsating may be observed.[1,2] There is some evidence to suggest that the aortic rupture itself is painless, and Sweet (cited by Copping[2]) suggested that the pain may be caused by blood tearing through the retroperitoneal tissues at aortic pressure.[2] In some cases the pain was such as to suggest renal disease.[3,4,5]

Recently I observed a patient with ruptured aortic aneurysm, whose only complaint following pain of short duration in the lower abdomen at the time of onset was pain in the testicle.

REPORT OF A CASE

The patient was a white man 59 years of age who twice had had coronary occlusion, first in January, 1953, and again in April, 1959. In January, 1957, cholecystectomy had been done for cholelithiasis. X-ray films of the chest taken at various times over the previous years had shown the heart to be of normal size and in transverse position. There was slight elongation and fusiform widening of the thoracic aorta. The patient's general health after the coronary occlusion in April, 1959, was considered good.

Then, on August 19, 1959, at 7:30 p.m., while eating dinner, he had a seizure of cramping lower abdominal pain with radiation to the right testicle. The pain was accompanied by profuse sweating and pronounced weakness. These symptoms lasted about ten to fifteen minutes. When examined at 8 p.m., the patient complained only of severe aching in the right testicle. There was no frequency or burning of urination and no blood in the urine. The temperature was 98° F., the heart rate 72, and the blood pressure 120/80 mm. of mercury. No tenderness was elicited over the kidneys, the abdomen or any part of the lower back. No muscular spasm or rigidity in the abdomen was noted. Despite the persistent pain in the testicle, it was not tender or abnormal in any observable way. The patient showed no signs of shock. For want of a better one, a diagnosis of possible renal calculus was considered. The patient was given 100 mg. of meperedine (Demerol) intramuscularly.

The only complaint continued to be persistent pain in the right testicle. An hour after onset of symptoms, the patient had a large bowel movement of brown, well formed stool. Shortly thereafter he vomited profusely.

At 10 p.m., generalized pallor developed, the blood pressure dropped to 90/70 mm. of mercury, and the pulse became rapid and thready. On further questioning the patient still spoke only of right testicular pain. A physical examination at this time was no more revealing than the one done earlier, except for shock. A diagnosis of ruptured aneurysm was considered.

An x-ray film of the abdomen showed complete obliteration of the right psoas shadow. The hematocrit was 45 per cent and the hemoglobin content was 14.7 gm. per 100 cc. of blood. Leukocytes numbered 17,800 per cu. mm.—91 per cent polymorphonuclear cells, (83 per cent segmented and 8 per cent stab forms), 6 per cent lymphocytes and 3 per cent monocytes. An electrocardiogram showed evidence of an old anteroseptal myocardial infarction, not changed from previous tracings.

The symptoms of shock deepened despite measures to alleviate it and the patient died at 11:30 p.m.

*Pathologist's Report.** At autopsy evidence of bleeding into the right retroperitoneal gutter was observed. A hemorrhagic mass at that site measured 20x10x8 cm. There was dissection of the hemorrhage into the mesentery of the colon, predominantly the ascending colon.

Calcific arteriosclerosis of the entire aorta, increasing in severity as the abdominal aorta was approached was noted. An aneurysm 10 cm. in diameter extended from just below the renal arteries to 1 cm. above the bifurcation of the aorta into the iliac vessels. It contained laminated clot (old), the unclogged lumen varying in size from 1 to 2 cm. On the right lateral surface of the inner wall of the aneurysm was a 2 cm. vertical defect which communicated with the previously described retroperitoneal hemorrhagic area. The hemorrhagic mass

Submitted September 28, 1959.

*Dr. Yosef Tiber.

surrounded the right kidney and the right ureter. The subscapular surface of the kidney showed numerous small pinpoint scars, suggestive of arterial disease, but the parenchyma appeared normal. The adrenal glands were not involved in the hemorrhagic mass.

The principal autopsy diagnoses were: (1) Ruptured abdominal aortic aneurysm with retroperitoneal hemorrhage; (2) arteriosclerosis of the kidneys; (3) arteriosclerosis of the coronary arteries and aorta.

SUMMARY

In the case of ruptured aneurysm of the abdominal aorta here reported, the predominant symptom was pain in the right testicle. There was neither tenderness in the abdomen and flanks nor a palpable mass in the abdomen. Not until the patient went into shock was the true diagnosis suspected.

8126 Beverly Boulevard, Los Angeles 48.

REFERENCES

1. Cooley, D. A., and DeBakey, M. E.: Ruptured aneurysms of abdominal aorta, Postgraduate Med., 16:334, 1954.

2. Copping, G. A.: Spontaneous rupture of abdominal aorta, J.A.M.A., 151:374, 1953.

3. Enselberg, C. D.: The clinical picture of aneurysm of the abdominal aorta, Ann. Int. Med., 44:1163, 1956.

4. Lazarus, J. A., and Marks, M. S.: Aneurysms of the abdominal aorta associated with urinary symptoms, J. Urol., 52:115, 1944.

5. Uhle, C. A. W.: The significance of aneurysm of the abdominal aorta masquerading as primary urologic disease, J. Urol., 45:13, 1944.

Adult Chickenpox Pneumonia

BERNARD JOFFEE, *M.D.*, San Francisco

PRIMARY VARICELLA PNEUMONIA in adults, previously reported as a rare disease,[2] was recently shown to be not uncommon in a series of adult cases of chickenpox.[1] The purpose of this report is to describe a case of adult varicella pneumonia, characterized by cyanosis and severe air hunger, and to indicate the importance of an x-ray film of the chest and careful thoracic examination in cases of chickenpox in adults.

REPORT OF A CASE

A 37-year-old white man was admitted to the 6510th USAF Hospital on May 27, 1958, because of severe shortness of breath. Two weeks before admission his 8-year-old child had had varicella, a disease the patient had not had as a child. He had had smallpox vaccination in 1957. Three days before admission a rash developed on the patient's forehead, face and trunk, then spread to his legs. Two days before admission he noted shortness of breath and cough productive of thin white sputum with occasional flecks of blood. Coughing grew constant, and shortness of breath became so severe that he presented himself to the hospital emergency room.

When examined, the patient, who was tall and well developed, was breathing shallowly and rapidly. The skin, nail beds and mucous membranes were cyanotic. A generalized eruption of mixed papules, vesicles and crusts typical of varicella was present. On the hard palate there was a small white vesicle. The entire lung fields were dull to percussion. Tactile and vocal fremitus were everywhere diminished, and medium moist, inspiratory and expiratory rales were heard anteriorly and posteriorly on both sides. All accessory muscles of respiration were being used.

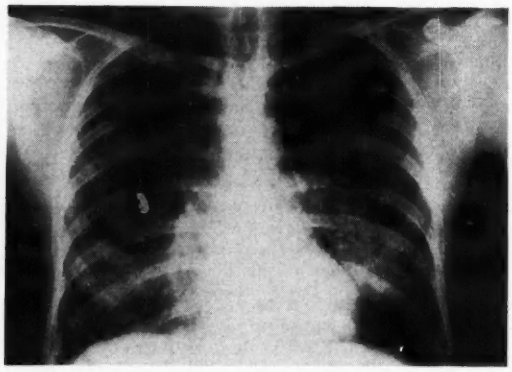


Figure 1.—The confluent and nodular nature of the generalized pulmonary infiltrate is shown in film taken at time of admission of patient to hospital.

The oral temperature was 102° F., the pulse rate 100 and the blood pressure 120/70 mm. of mercury.

Hemoglobin was 14 gm. per 100 ml. of blood. Leukocytes numbered 5,400 per cu. mm.—39 per cent neutrophils and 54 per cent lymphocytes. Results of urinalysis were within normal limits. A mixed flora was observed on microscopic examination of the sputum and no pathogens grew on a culture. Cultures of two specimens of blood taken the day of admission showed no growth. Cold agglutinins showed no titer the day of admission or two weeks later. Serum taken in the acute and the convalescent phases (studied at the California State Department of Public Health, Viral and Rickettsial Disease Laboratory, Berkeley) showed no significant titer or rise in titer for psittacosis, Q fever, adenovirus, coxsackie, influenza A and B, or the lymphogranuloma venereum group. An x-ray film of the

Submitted July 22, 1959.

chest showed a confluent nodular infiltrate throughout both lung fields.

The patient was placed in an oxygen tent in orthopneic position and treated with penicillin and streptomycin until the reports of no growth of blood and sputum cultures were received. Tachypnea and cyanosis steadily decreased and supplementary oxygen was discontinued eight days after admission. Serial x-ray films indicated a change from a nodular to a linear lung infiltrate. He was discharged June 23, 1958, and remained well, with no abnormalities in x-ray films of the chest.

DISCUSSION

Forty-five cases of adult varicella had been reported in the literature previous to the present case. Although the pneumonia complicating childhood chickenpox is generally bacterial,[3] it is almost always viral when it occurs in adults. Postmortem examinations of adults who died of chickenpox have revealed typical pathological lesions of chickenpox in the lungs.[2] Dyspnea and cyanosis result from gross involvement of lung tissue and interference in oxygen exchange because of cellular debris present in the alveoli. On x-ray films the infiltrate often appears confluent and nodular.

Once proper studies have been performed to rule out bacterial cause of the pneumonia, symptomatic care with oxygen and maintenance of orthopneic position should be given. Antibiotics are futile.

2340 Filbert Street, San Francisco.

REFERENCES

1. Hampton, A. G., Jr.: Primary varicella pneumonia, Arch. Int. Med., 95:137-140, 1955.

2. Krugman, S., Goodrich, C. H., and Ward, R.: Primary varicella pneumonia, New Eng. Med., 257:843-848, 1957.

3. Weinstein, L., and Meade, R. H.: Respiratory manifestations of chickenpox: Special considerations of features of primary varicella pneumonia, Arch. Int. Med., 98:91-99, 1956.

The Familial Occurrence of Chronic Lymphocytic Leukemia and Multiple Myeloma

SAMUEL K. WIRTSCHAFTER, M.D., and SAMUEL I. RAPAPORT, M.D., Los Angeles

THE REPORT herewith is of the occurrence of chronic lymphocytic leukemia in a mother and multiple myeloma in one of her two sons. We have not been able to find a previous report of the presence of these two hematologic malignant diseases in the same family.

CASE 1. The patient, an 84-year-old white woman, was first observed at the Los Angeles County General Hospital in 1955 because of vague, generalized pain which had been present for many years. A diagnosis of chronic lymphocytic leukemia had been established by lymph node biopsy at another hospital in 1942. At that time leukocytes numbered 22,000 per cu. mm., 76 per cent lymphocytes. The diagnosis had been confirmed in 1950 by bone marrow examination and liver biopsy at the same hospital. Examination of the blood in 1953 showed 80,000 leukocytes per cu. mm., 95 per cent lymphocytes.

Upon physical examination in 1955 the patient was observed to be well developed and well nourished. Moderate cardiomegaly and auricular fibrillation were present. The edge of the liver was palpated one or two finger breadths below the right costal margin and the spleen two to three finger breadths below the left costal margin. There was no enlargement of peripheral lymph nodes. The hemoglobin content was 12 gm. per 100 cc. of blood and leukocytes numbered 48,400 per cu. mm., 90 per cent of them mature lymphocytes.

Between 1955 and 1959 the patient was observed from time to time in the outpatient medical clinic with occasional admission to the hospital for management of heart disease. The liver and spleen shrank during that time and were no longer palpable. Enlarged peripheral lymph nodes were never felt. The hemoglobin content varied between 10 and 12 gm. per 100 cc. and the number of leukocytes between 60,000 and 100,000 per cu. mm.

In March, 1959, the hemoglobin fell to 7.0 gm. per 100 cc. and the number of leukocytes rose to 118,000 per cu. mm. Two units of whole blood were given but the patient died about three weeks later. Autopsy was not done.

It is noteworthy that this patient did not receive specific antileukemic therapy at any time during the 17 years she was known to have lymphocytic leukemia.

CASE 2. The 51-year-old son of the patient in Case 1 entered Los Angeles County General Hospital in December, 1958, because of skeletal pain associated with osteolytic lesions demonstrated on roentgenograms taken by a physician he had consulted. The only abnormality noted on physical examination was tenderness over the thoracic and lumbar vertebrae and over the upper extremities. The hemoglobin content was 14.0 gm. per 100 cc. of blood and leukocytes numbered 8,400 per cu. mm. with a differential count on stained smear within normal limits. Urinalysis revealed 4+ proteinuria and Bence-Jones protein. The serum protein contents were within normal range. Roentgenograms showed multiple osteolytic lesions of the calvarium, humeri, radii,

From the Medical Service, Los Angeles County General Hospital (Wirtschafter) and the Department of Medicine, University of Southern California School of Medicine (Rapaport).

ribs and vertebrae. Microscopic examination of a specimen of bone marrow was consistent with a diagnosis of multiple myeloma with a large number of plasma cells, some with nucleoli.

Family Data

The patient in Case 2, who has no children, has one sibling, a brother, who has been examined by us and who has no evidence of hematologic disease, and his one daughter and one grandchild are reported to be well.

Comment

The familial occurrence of leukemia has been well demonstrated. Videbaek[9] compiled from the literature and from his own observations 86 authenticated cases of leukemia in 39 families. He also noted the co-existence of leukemia and cancer in the same patient and the higher incidence of cancer in the family members of leukemic patients when compared with a group of control families. Videbaek suggested, on the basis of his studies, that there exists a strong constitutional familial predisposition toward neoplastic disease. He found that, unlike cancer, the hematologic abnormalities of pernicious anemia, hemophilia and polycythemia vera were no more common in leukemic patients and their families than in normal controls.

Numerous other reports have appeared documenting the familial occurrence of leukemia. Anderson's[1] paper is noteworthy in that it reports the presence of lymphocytic leukemia in five of eight siblings. Gunz and Dameshek[3] noted the occurrence of lymphocytic leukemia in twin brothers and the subsequent development of a similar type of leukemia 25 years later in the son of one of these men.

Dameshek and Gunz[2] recently reviewed the role of heredity in leukemia. They called attention to a possible difference in the different types of leukemia and pointed out that most of the (about) 100 reported cases of familial leukemia are of the lymphocytic variety. They conclude that heredity may play an important part in the genesis of lymphocytic leukemia and lymphosarcoma, but may not be important for the other types of leukemia. It is of interest, in this connection, that lymphocytic leukemia is almost non-existent in the Japanese.

Schier[8] reviewed the several published examples of familial Hodgkin's disease and himself reported two instances of familial occurrence. Hennessy and Rottino[4] discussed the uncommon occurrence of Hodgkin's disease in children born of women who had the disease during pregnancy.

Familial multiple myeloma is apparently very rare. Only four well-documented cases of myeloma in close relatives have been reported. Mandema and co-workers[6] in 1954 published the first report of its occurrence in siblings. Nadeau and co-workers[7] described three cases of multiple myeloma in three members of two generations of the same family. Herrel, Ruff and Bayrd[5] found multiple myeloma in two brothers. The most recent example appeared in a case record of the Massachusetts General Hospital.[10]

The cases here reported are the first we know in which multiple myeloma and chronic lymphocytic leukemia have been found in close relatives. This may reflect a predisposition toward malignancy in this family, but, of course, may also be a coincidence. It is important for medical practitioners to document such occurrences as a prerequisite to the assessment of the role of heredity in human neoplasms.

The mother's case history illustrates an important point, namely, that a 17-year survival can occur in chronic lymphocytic leukemia without anti-leukemic therapy. This emphasizes again that all cases of chronic lymphocytic leukemia do not require therapy at the time the diagnosis is discovered. Indeed, an occasional patient, usually elderly, lives for many years with lymphocytic leukemia before treatment is indicated.

2025 Zonal Avenue, Los Angeles 33 (Rapaport).

REFERENCES

1. Anderson, R. C.: Familial leukemia: A report of leukemia in five siblings with a brief review of the genetic aspects of this disease, Am. J. Dis. Child., 8:313-322, March 1951.

2. Damashek, W., and Gunz, F.: Leukemia, Grune and Stratton, New York, 1958.

3. Gunz, F., and Damashek, W.: Chronic lymphocytic leukemia in a family, including twin brothers and a son, J.A.M.A., 164:1323-1325, July 20, 1957.

4. Hennessey, J. P., and Rottino, A.: Hodgkin's disease in pregnancy with report of twelve cases, Am. J. of Obst. and Gynecol., 63:756-764, April 1952.

5. Herrell, W. E., Ruff, J. D., and Bayrd, E. D.: Multiple myeloma in siblings, J.A.M.A., 167:1485-1487, July 19, 1958.

6. Mandema, E., and Wildervanck, L. S.: La Maladie de Kahler (Myeloma Muliples) chez deux soeurs, J. de Genet. humaine, 3:170-175, 1954.

7. Nadeau, L. A., Magalini, S. I., and Stefanini, H.: Familial multiple myeloma, Arch. Path., 61:101-106, 1956.

8. Schier, W. W.: Familial Hodgkin's disease, Blood, 9:236-240, March 1954.

9. Videbaek, A.: Heredity in human leukemia and its relation to cancer, Ejmar Munksgaard Forley, 149, Vol. 13, Busck, Copenhagen, 1947.

10. Case 45261, Case records of the Massachusetts General Hospital, New Eng. J. Med., 260:1336-1342, June 25, 1959.

California MEDICINE

For information on preparation of manuscript, see advertising page 2

EDITORIAL

A Million Dollars for Medical Education

CASH CONTRIBUTIONS to medical schools in the United States made by the California Medical Association in the past ten years have come to almost a million dollars.

Medical schools throughout the country, along with everybody else, have suffered in recent years from the effects of inflation. The costs of educating students have risen in proportion with other costs. Salaries have advanced, equipment and building costs have grown and expenses in all departments have followed the upward trend of general prices.

Coupled with these increased costs, the medical schools have often found themselves facing boards of trustees of large universities where the losses on medical training cannot be adequately made up by surpluses in other colleges or by increased endowment income. In these circumstances it was not unexpected that some medical school deans announced themselves in favor of federal subsidies to medical schools.

It is fortunate that some farsighted medical educators, working in conjunction with business interests, established both the American Medical Education Foundation and the National Fund for Medical Education some ten years ago. The AMEF, whose administrative costs are paid by the American Medical Association, collects contributions from physicians and pays them out to the medical schools. The same procedure is followed by the National Fund, except that its source of income is business and industry.

The California Medical Association was among the earliest state medical organizations to grasp the significance of these funds and to arrange to support them. Under the California program, each member of the Association contributes a small sum each year as part of his C.M.A. dues. The proceeds are turned over to the AMEF, 80 per cent earmarked for the three California medical schools which are not primarily tax-supported, the balance for the general fund to go equally to all medical schools.

While the contribution of the individual member (ten dollars a year, tax-deductible) is not great, the aggregate comes to a neat sum. In 1959, the Association contributed more than $156,000 in this manner. The three private schools in California received close to $42,000 each from this one source.

This annual effort represents medical organizations at their best—members of a profession contributing to the education of those who will follow them, even compete with them.

Medical education must be continued and must be strengthened. Federal funds which carry policy-making strings must be eschewed. The picture of today's physicians helping train tomorrow's is a pleasant sight and, we hope, a permanent monument to a graceful tradition.

Physicians and Population

"POPULATION EXPLOSION" is a term that has come into prominence in recent months.

In California, it is now quite obvious that the five medical schools in the state will not be able for some years to come to produce enough new physicians to meet the demands of a sharply increasing population.

Attention of the medical and the educational world has been focused on this problem in recent weeks through the publication of a treatise on "The West's Medical Manpower Needs." The volume comes from the Western Interstate Commission for Higher Education, popularly known as WICHE.

WICHE is the cooperative group of western educators who plan for the higher (professional) education of the youth of the 13 states making up the

organization. These are the Rocky Mountain and Pacific states plus our new neighbors, Hawaii and Alaska.

In its new publication WICHE looks at population forecasts for this region up to the year 1975. It analyzes the capacity of these states to produce medical graduates and to provide them in their own areas. It goes into the medical manpower needs of the western area and considers all elements which may call for more or fewer physicians per population unit.

Basically, the report finds that the western states are due for a tremendous gain in population between now and 1975, that the present medical schools in the area will fall far short of producing enough physicians to care for the anticipated population and that plans should be initiated now for educating and otherwise acquiring more physicians for the immediate future.

Population increases from 1955 to 1975 are estimated in this study to run from as little as 22 per cent for Montana to as high as 158 per cent for Nevada. California, the state with by far the largest population in the area, is expected to have 23,565,000 people by 1975, or close to 88 per cent ahead of 1955 figures.

In the chapters on how many physicians are needed to serve today's population, the WICHE study shows a 1955 average of about 140 physicians per 100,000 population. California topped that figure considerably, with 159 physicians per 100,000. In 1957 this figure had dropped to 157 as the state's population continued its rapid expansion. To maintain the 1955 ratio, California will need a net increase of some 13,000 physicians by 1975.

It is interesting to note that estimates of physicians required to serve the 1975 population are based primarily on the individual opinions of the medical and educational experts making up the WICHE study team. The advent of new drugs, more effective therapy, more widespread use of technicians and other factors are expected to make it possible for one physician to serve more people. On the other hand, the study shows that "more people want more medical service" and are able to pay for it.

California's physician-to-population ratio today shows one physician for about every 640 people. During World War II the War Manpower Commission ordered that no community should have its physicians depleted below an average of one to each 1,500 people. Even so, in some areas the ratio ran as high as one per 3,000. Fortunately, there were no major outbreaks of disease to strain these overloaded ratios but, conversely, the physicians remaining in their communities at that time managed to handle their added professional load in splendid fashion, even though many of them were the older men, the physically handicapped and others who were deemed least suited for military service.

These figures, not included in the WICHE study, may serve as a background of comparison with the estimates made in this survey.

If the WICHE estimates are correct, the California Medical Association may look forward to a 1975 membership of about 30,000, a figure which appears acceptable in the light of annual C.M.A. membership gains in recent years. A net membership increase of four per cent a year would bring C.M.A. membership close to 31,000 in 1975; the Association has actually enjoyed an average annual gain of more than four per cent net in recent years.

Reflection on these forecasts must revert to recent experience in California, where medical population has been growing along with the general populace. In the five-year period 1954-1958, the state licensed an average of 2,032 physicians a year. Of these, only 281, on the average, were graduates of California medical schools. About half those licensed each year come to California through reciprocity licenses in other states, and about one-quarter are diplomates of the National Board of Medical Examiners whose credentials are acceptable here.

These statistics would seem to indicate that where the general population increases, the medical population does likewise. The physician-to-population ratio in the state has not varied much in the past 20 years. To reduce the matter to extremely general language: Every time 650 people come to California from other areas they bring one physician with them.

In light of the inability of California's medical schools to train enough new physicians to meet the growing needs, and with a quite practical consideration of the cost to our state even if more could be trained, this tendency of new population to attract physicians who were trained elsewhere is one that we as taxpayers may welcome.

Where gaps exist in medical manpower, foreign graduates help to fill them. However, this is not true to any great extent in California, which has been slow to accept many foreign medical men. This aspect may well be discounted in our current consideration of medical needs, at least as far as this state is concerned.

Medical education requires many years, especially where the graduate chooses a specialty and takes two to five years' additional training following the internship year. For this reason, and because the establishment or expansion of a medical school requires additional years of planning, WICHE suggests looking ahead 15 years to the time when new medical graduates may be expected from new

schools or expanded programs in our present schools. Its study shows the need of both new schools and larger classes in the schools we already have.

In view of the certain prospect of population increases in the western area in the coming years, in view of the need for additional physicians to serve this population, and in view of the years of advance planning needed to fill this demand for medical care, the WICHE study is most timely. Even if some may argue with the estimate of the ability of one physician to serve more or fewer patients as time goes on, it is obvious that we will need more physicians in California to serve the ever-growing population. Plans must be made at once for action to take place later. It is to be hoped that we have not already waited too long to plan for an orderly program.

Letters to the Editor...

Physical Examinations for Physicians

WE ARE CERTAIN that the following information merits publication in CALIFORNIA MEDICINE since it is obviously a matter of general interest to your readers.

On August 12, 1959, the Culver City Hospital instituted a program of physical examinations for all professional members of the staff. This program includes a complete physical examination, x-ray of the chest, electrocardiographic study, complete blood count, urine analysis, serology, blood sugar and cholesterol estimation.

In addition, where chief complaints warrant, additional laboratory and x-ray studies are conducted.

It should be emphasized that the basic physical and laboratory procedures, along with any additional studies, are conducted completely free of charge.

It is interesting to note that according to the examining doctors at least 20 per cent of the physicians undergoing these examinations have additional x-ray and laboratory examinations. To our knowledge no other hospital in Southern California has undertaken this program.

The success of this program to date has been most satisfactory inasmuch as 50 per cent of the staff members have already availed themselves of the opportunity of these voluntary checkups.

The committee in charge of this program consists of F. H. Blanchard, M.D., Louis Paddie, M.D., Milton Rosenthal, M.D., J. G. Conti, Jr., M.D., Samuel Steinberg, M.D., Alfred Conti, M.D., and Sidney Messer, M.D., chairman.

Sincerely,
DAVID M. BROTMAN, M.D.,
Medical Director, and
JAMES G. CONTI, JR., M.D.,
President of Staff, Culver City Hospital

California MEDICAL ASSOCIATION

NOTICES & REPORTS

Council Meeting Minutes

Minutes of the 454th Meeting of the Council, Canterbury Hotel, San Francisco, December 12, 1959.

The meeting was called to order by Chairman Lum in the English Room of the Canterbury Hotel, San Francisco, on Saturday, December 12, 1959, at 9:30 a.m.

Roll Call:

Present were President Reynolds, President-Elect Foster, Speaker Doyle, Vice-Speaker Heron, Secretary Hosmer, Editor Wilbur and Councilors MacLaggan, Wheeler, Todd, Quinn, O'Neill, Kirchner, O'Connor, Shaw, Gifford, Harrington, Davis, Sherman, Campbell, Lum, Bostick and Teall.

Quorum present and acting.

Present by invitation were Messrs. Hunton, Thomas, Clancy, Collins, Marvin, Whelan and Dr. Batchelder of C.M.A. staff; Messrs. Hassard and Huber of legal counsel; Eugene Salisbury of staff and the Public Health League of California; John Fraser of the Public Health League; county society executives Scheuber of Alameda-Contra Costa, Geisert of Kern, Pettis and Field of Los Angeles, Brayer of Riverside, Donmyer of San Bernardino, Nute of San Diego, Thompson of San Joaquin, Dochterman of Sacramento and Dermott of Sonoma; Dr. A. E. Larsen and Messrs. Paolini, Lyon and Virello of California Physicians' Service; Dr. L. E. Osgood and Mr. M. R. Karstaedt of Visalia; Dr. John Morrison, president of the Alameda-Contra Costa Medical Association; Dr. Robert Holmes, president of the San Mateo County Medical Society; Dr. Daniel Blaine, Director of the State Department of Mental Hygiene; Dr. Malcolm Merrill, Director of the State Department of Public Health; and Dr. John Keye, medical director of the State Department of Social Welfare; Dr. Russell Ferguson, health officer of Santa Cruz County, and Doctors Dan O. Kilroy, Thomas Elmendorf and Francis E. West.

1. *Minutes for Approval:*

On motion duly made and seconded, minutes of the 453rd Council meeting, held October 31, 1959, were approved.

2. *Membership:*

(a) A report of membership as of December 10, 1959, was presented and ordered filed.

(b) On motion duly made and seconded, 87 members who had become delinquent and subsequently paid their dues were voted reinstatement.

(c) On motion duly made and seconded, Doctor Bernice I. Swenson of Alameda-Contra Costa County, was voted Retired Membership.

(d) On motion duly made and seconded in each instance, four applicants were voted Associate Membership. These were: Bernhard G. Anderson, Loren W. Heather, Carol E. Query, Orange County; Clark Richardson, Tulare County.

(e) On motion duly made and seconded, reductions of dues were voted for six members because of illness or postgraduate study.

3. *Liaison Committee to Social Welfare:*

Dr. Sherman reported that the Liaison Committee to the State Department of Social Welfare had discussed with Dr. Russell Ferguson, public health officer of Santa Cruz County, a program which he

has initiated there, to provide a plan of hospitalization for surgery, plus dental care, to recipients of aged and needy blind benefits. Dr. Ferguson intends to present this plan to the State Department of Social Welfare for possible use in other areas. The Liaison Committee has referred the plan to Dr. Batchelder, Mr. Whelan and Mr. Lyon of C.P.S. for study. On motion duly made and seconded, this procedure was approved.

Dr. Sherman also reported on Resolution No. 43 from the 1959 House of Delegates. This called for federal and state funds to be used for the purchase of health insurance for welfare recipients. Inasmuch as a pilot program of this type is under way in Glenn County, the committee felt that the intent of the resolution was being met and that no further action was needed at this time. On motion duly made and seconded, this procedure was approved.

Discussion was held on a manual prepared by welfare authorities as a screening guide in categorizing diagnoses of illness. On motion duly made and seconded, it was voted to oppose the use of this type of guide by nonmedical personnel.

4. *Report of the President:*

President Reynolds reported on recent meetings he had attended in Honolulu and Minneapolis on the subject of prepayment medical care plans. He also requested advice from the Council on a letter which had been voted at the previous meeting to be prepared for all Association members over his signature. Two proposed drafts of this letter were presented and reviewed. Letters from several county societies, including Los Angeles, Alameda-Contra Costa and San Diego, were read by members. On motion duly made and seconded, it was voted that draft "A" of the proposed letter be sent to all C.M.A. members over Dr. Reynolds' signature.

5. *Report of the President-Elect:*

Dr. Foster reported on the recent A.M.A. meeting in Dallas and on a conference staged by the A.M.A. Council on Medical Service in conjunction with the meeting, at which various medical care programs were reviewed.

6. *Finance Committee:*

Dr. Heron presented a new form of financial report, showing the net asset value of the Association and its allied organizations, including Trustees of the C.M.A., Physicians' Benevolence Fund, Inc., Audio-Digest Foundation and Pacific Magnetic Tape Equipment Co. It was announced that such reports would be provided at quarterly intervals.

Mr. Hunton explained the necessity of borrowing funds in the final months of the year and suggested that where the Trustees of the C.M.A. or Physicians' Benevolence Fund had available funds, such borrowing be made from them at prevalent interest rates for short-term investments rather than from banks at higher rates. On motion duly made and seconded, this procedure was voted approval.

7. *Woman's Auxiliary:*

A request from the Woman's Auxiliary for the appropriation of additional funds for publication of its *Courier* was presented and referred to the Finance Committee because of the additional money involved.

8. *Committee on Nominations:*

Dr. Bostick reported that nominations were soon due for vacancies on the Board of Trustees of California Physicians' Service. On motion duly made and seconded, approval was voted for the following nominees: Dudley M. Cobb, Jr., M.D., Los Angeles; Mr. Ransom M. Cook, San Francisco; John R. Hilsabeck, M.D., Santa Ana; John G. Morrison, M.D., San Leandro; Herman H. Stone, M.D., Riverside.

Dr. Bostick also suggested the advisability of naming committees to serve under the Cancer Commission. On motion duly made and seconded, this proposal was approved.

On motion duly made and seconded, it was voted that the present *ad hoc* Committee on Traffic Safety constitute this committee until the 1960 Annual Session and that it report to the Council before that time.

9. *Commission on Medical Services:*

Mr. Hassard referred to an earlier Council action which requested immediate action on implementing the provision of adequate medical and allied care for older citizens; he reported that Messrs. Salisbury and Fraser were now visiting county societies to alert them to the need of compiling inventories of facilities available for the aged group. These visits will be followed by visits from staff members, who will assist the county societies in gathering and compiling the necessary information for such studies. On motion duly made and seconded, it was voted to approve this procedure in principle.

10. *Commission on Community Health Services:*

Dr. MacLaggan reported that some of the services which had been eliminated from the "Medicare" program were now being restored and that military dependents benefiting from this program would be allowed free choice of physician in many instances under the new regulations.

11. *Commission on Public Policy:*

Dr. Dan O. Kilroy, chairman of the Commission on Public Policy, and Dr. Malcolm Watts, chairman

of the Committee on Public Relations, reported on a meeting held the previous day, at which discussion was held on a proposed program of public relations.

Mr. Hassard discussed a study which had been made on possible means of complying with the intent of Resolution No. 18 from the 1959 House of Delegates, which suggested the employment of outside public relations counsel. The resolution was referred to the Commission on Public Policy, which will make a further report.

Mr. Eugene Salisbury outlined a campaign of correspondence for the use of physicians in opposing federal legislation deemed inimical to the interests of the profession.

President Reynolds read an editorial from a San Francisco newspaper which suggested the removal of earnings limitations on recipients of Social Security benefits. On motion duly made and seconded, he was authorized to write to the paper and to Representative Curtin of Pennsylvania to indicate that the Association approves this type of legislation.

12. *State Department of Public Health:*

Dr. Malcolm Merrill reported that Governor Brown had named the members of the Cancer Advisory Council and of the Citizens Committee on the Health Needs of the People.

13. *Commission on Medical Education:*

On motion duly made and seconded, approval was voted for two proposals submitted by the Commission on Medical Education.

On motion duly made and seconded, approval was voted to reduce the registration fees for postgraduate institutes to $15 a member.

On motion duly made and seconded, approval was voted for a decision of the Committee on Scientific Work to oppose the creation of a new scientific section dealing with chest diseases.

A list of nonmembers to appear on the 1960 Annual Session program was presented and approved. On motion duly made and seconded, the staff was instructed to prepare By-Law amendments to eliminate the necessity of the Council supervising the list of guest speakers.

14. *Tulare County Medical Society:*

Dr. L. E. Osgood of Visalia reported on the formation in his area of the American Patients' Association, a cooperative organization sponsored by college faculty members. On motion duly made and seconded, it was voted to offer assistance to the Tulare County Medical Society, under the supervision of the Commission on Medical Services, in observing this development.

Adjournment:

There being no further business to come before it, the meeting was adjourned at 5:15 p.m.

DONALD D. LUM, M.D., *Chairman*
MATTHEW N. HOSMER, M.D., *Secretary*

In Memoriam

BRUST, PAUL RAYMOND. Died in San Diego, December 24, 1959, aged 65. Graduate of Stanford University School of Medicine, Stanford-San Francisco, 1926. Licensed in California in 1926. Doctor Brust was a member of the San Diego County Medical Society.

KOHLMOOS, HENRY J. Died in Piedmont, December 5, 1959, aged 94, of bronchopneumonia. Graduate of Hessische Ludwigs-Universitat Medizinische Fakultat, Giessen, Hesse, Germany, 1893. Licensed in California in 1896. Doctor Kohlmoos was a retired member of the Alameda-Contra Costa County Medical Association and the California Medical Association and an associate member of the American Medical Association.

MARCUS, JOSEPH HARVEY. Died in Los Angeles, December 24, 1959, aged 57. Graduate of Tufts University School of Medicine, Boston, Massachusetts, 1929. Licensed in California in 1930. Doctor Marcus was a member of the Los Angeles County Medical Association.

PERELSON, HAROLD NATHAN. Died December 6, 1959, aged 50. Graduate of State University of New York College of Medicine at New York City, Brooklyn, N. Y., 1935. Doctor Perelson was a member of the Los Angeles County Medical Association.

RUSSELL, RALPH SWISHER. Died in La Jolla, December 10, 1959, aged 59. Graduate of University of Nebraska College of Medicine, Omaha, 1925. Licensed in California in 1939. Doctor Russell was a member of the San Diego County Medical Society.

WORTHINGTON, LOIS CLAIR. Died in Bakersfield, December 20, 1959, aged 84. Graduate of Cooper Medical College, San Francisco, 1897. Licensed in California in 1898. Doctor Worthington was a member of the Kern County Medical Society.

YOCOM, FRANK WILLIS. Died December 29, 1959, aged 75. Graduate of University of California School of Medicine, Berkeley-San Francisco, 1922. Licensed in California in 1922. Doctor Yocom was a member of the Los Angeles County Medical Association.

10th ANNIVERSARY

POSTGRADUATE INSTITUTE

NORTH COAST COUNTIES

Presented by College of Medical Evangelists, G. E. Norwood, M.D., Assistant Dean and Chairman of the Division of Postgraduate Medicine, and California Medical Association Committee on Postgraduate Activities.

Varying methods of presentation will be used including the most recent audio-visual techniques.

Flamingo Hotel, Santa Rosa

March 31 and April 1

PROGRAM

THURSDAY, MARCH 31

Morning Session

Therapeutics

9:00-9:30—**Recent Developments in Hemopoetic Agents**—C. Joan Coggin, M.D.

9:30-10:15—**Anatomy and Physiology of the Skin as Related to Standard and New Dermatomucosal Therapeutic Agents**—Clement E. Counter, M.D. (Last 20 minutes a panel discussion.)

10:15-10:45—**Recent Advances in the Therapy for Toxemia of Pregnancy**—Ervin E. Nichols, M.D.

11:00-11:45—**Panel: Specific Laboratory Diagnosis of Thyroid Disease with Well-Defined Indications for Thyroid Therapy.**

11:45-12:15—**When Is Thyroid Surgery to Be Done?**—Arthur C. Miller, M.D.

Afternoon Session

Geriatrics—Section 1

2:00-3:00—**Geriatrics and Rehabilitation Clinic**—John E. Affeldt, M.D. (Cases from Santa Rosa.)

3:00-3:30—**Geriatric Urology**—Roger Wm. Barnes, M.D.

3:45-4:30—**A Trip Through the Kidney**—C. Joan Coggin, M.D.

4:30-5:00—**Panel Discussion and Question and Answer Period.**

Obstetrics and Gynecology—Section 2

2:00-3:00—**When Is Endometriosis a Surgical Problem?**—G. E. Norwood, M.D.

2:30-3:00—**Surgical Complications of Pregnancy**—Ervin E. Nichols, M.D.

3:00-3:30—**The Impact of Surgery on the Patient's Metabolism**—Edward R. Bloomquist, M.D.

3:45-4:30—**Diagnosis and Management of Bleeding in the Three Trimesters of Pregnancy**—Ervin E. Nichols, M.D.

4:30-5:00—**Panel Discussion and Question and Answer Period.**

FRIDAY, APRIL 1

Morning Session

The Breast

9:00-9:45—**Anatomy and Physiology of the Breast—Significance of Cyclic Changes and Such States as Adenosis**—G. E. Norwood, M.D.

9:45-10:30—**Diagnosis and Surgical Management of Benign Tumors of the Breast**—Arthur C. Miller, M.D.

Surgery—Section 1

10:45-11:30—**How to Select Patients for Heart Surgery**—C. Joan Coggin, M.D.

11:30-12:15—**Recent Developments in Anesthesia and New Pharmacological Adjuncts**—Edward R. Bloomquist, M.D.

Dermatology—Section 2

10:45-12:15—**Dermatological (Wet) Clinic and Demonstration of Therapeutic Modalities and Minor Office Surgery**—Clement E. Counter, M.D.

Afternoon Session

2:00-2:45—**Pediatric Urology**—Roger Wm. Barnes, M.D.

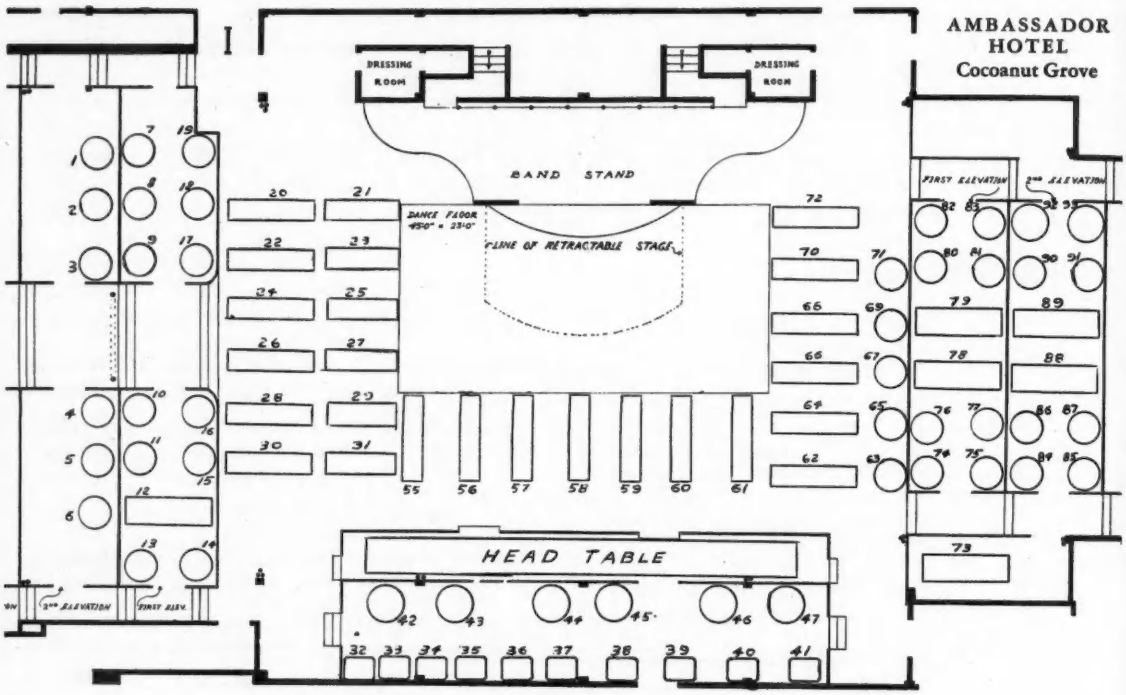
2:45-3:30—**Panel: Energetics (the Metabolism of Energy) and Its Relationship to Fatigue—Obesity—Psychosomatics.**

3:30-4:30—**Summary of Session and Final Question and Answer Period.**

HOST: Sonoma County Medical Society . . . **REGIONAL CHAIRMAN:** H. Ward Wick, M.D., 858 Fourth Street, Santa Rosa. **INSTITUTE FEE:** $15.00. For additional information contact Postgraduate Activities office, California Medical Association, 2975 Wilshire Boulevard, Los Angeles 5. **All California Medical Association members and their families are cordially invited to attend.**

COME to the...

ANNUAL SESSION



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GO to the...

Presidents' Dinner-Dance

SUNDAY, FEBRUARY 21, 8 p.m.

Cocoanut Grove

Entertainment: LENA HORNE

Music for Dancing: DICK LA SALLE

Food: Prime Rib Dinner

Cost: $12.50 per person including tax, tip and cover

TICKETS ARE NOW ON SALE—USE COUPON BELOW

Your tickets will be held for you at the door. A receipt for your check will be sent to you. Please present this receipt at the door for your ticket, Sunday night.

OR

Tickets may be picked up at any time Sunday morning or afternoon, February 21, at ticket booth, Woman's Auxiliary registration desk. Requests for tables for large parties should be sent in one envelope and early.

MISS LOUISE KALINICH
Los Angeles County Medical Association
1925 Wilshire Boulevard
Los Angeles 57, California

Enclosed is my check for $_____. Please send me_____ticket(s) to the PRESIDENTS' DINNER-DANCE, Sunday, February 21, 1960.

Table Choice_____ _____ _____ —or assign next best available_____
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Address_____

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(Make checks payable to the California Medical Association)

PUBLIC HEALTH REPORT

MALCOLM H. MERRILL, *M.D., M.P.H.*
Director, State Department of Public Health

INFLUENZA and influenza-like illness spread to several areas in the state during January, particularly in Los Angeles, Fresno and Merced counties.

The department's Viral and Rickettsial Disease Laboratory has identified A-2 (Asian strain) influenza virus from patients in Stanislaus, Kern, San Bernardino, San Diego, Fresno and Orange counties.

While there has been nothing unusual reported from northern California, word was beginning to filter in on above-average school absenteeism as this report was being written. Two school districts in Santa Clara County reported absenteeism is up to 14 per cent, as compared with 8 per cent normally, and absenteeism is running between 10 and 12 per cent in Contra Costa County.

The department has recommended immunization with polyvalent vaccine including Asian strains for persons for whom onset of influenza might represent an added health risk, such as individuals with cardiovascular or pulmonary conditions, persons with chronic illness of any type, and pregnant women. It might also be wise to immunize key community personnel, such as communications workers, firemen and policemen, and health forces.

* * *

In mid-November the Bureau of Acute Communicable Diseases began to receive reports indicating an increasing incidence of gastrointestinal disease. The disease is characterized by nausea, vomiting and diarrhea usually lasting from one to three days. It has been severe enough in some infants to require hospitalization.

Twelve health jurisdictions have reported illness of this type: Alameda, Colusa, Los Angeles, Merced, Napa, Sacramento, Santa Clara, Shasta and Sonoma counties and the cities of Long Beach, Los Angeles and Pasadena.

The cities of Los Angeles and Long Beach and Shasta County have noted increased absenteeism in schools related to gastrointestinal illness. Two outbreaks have occurred in homes for the aged.

Bacteriologic studies in these two homes, and in two other outbreak areas, have all been negative for the usual pathogens. Similar epidemics of such disease with negative bacteriologic studies have led to suggestion that a virus is the etiologic agent.

The State Health Department's Viral and Rickettsial Disease Laboratory is attempting viral isolation from the two outbreaks. No further specimens for viral work are requested at this time. However, information concerning outbreaks is needed, and will be useful in describing the geographic and temporal distribution of the disease.

* * *

A study of the metabolism of zinc in persons with liver damage will be continued by the department for the next three years under a $55,000 grant awarded by the National Institutes of Health.

Dr. Wendell R. Lipscomb, chief of the Study and Investigation Section of the Division of Alcoholic Rehabilitation, and Dr. Harold L. Helwig, chief of the Air Sanitation and Industrial Hygiene Laboratory, in 1959 instituted the study after Harvard researchers and others reported that excretion of zinc is increased in animals and humans with cirrhosis of the liver. This trace metal is essential for the function of several enzymes of the body.

Preliminary work in the department has included development of improved methods for the analysis of zinc and confirmation that the metabolism of this trace metal is altered by liver malfunction. The federal grant will support a joint laboratory and epidemiological investigation of the occurrence of liver cirrhosis in selected populations of the state.

* * *

It happened again in 1959—a new record high in baby production, some 356,000 live births, a rate of 23.3 per 1,000 population. This is an increase of 7,000 over the year before.

The number of deaths is estimated at 128,000, an increase of 2,000 over 1958. With the state's increased population taken into account, this gives a rate of 8.4 per 1,000 population, a decrease in last year's rate of 8.5. It is estimated there were 47,000 deaths from heart disease, 21,000 from cancer, and 8,000 from accidents.

Provisional information indicates there were 102,000 marriages in California during 1959, a rate of 6.7 per 1,000 population, higher than the rate of 6.5 recorded in 1957 and 1958.

* * *

Dr. Harold M. Erickson on January 4 assumed his duties as new deputy director. Dr. Erickson had been director of the Oregon State Health Department since 1945. He fills the vacancy left by the death of Dr. Frederic M. Kriete in July.

* * *

Under a mandate from the 1959 Legislature, the

Bureau of Crippled Children Services is undertaking a four-year study and pilot program in the field of medical care for children suffering from epilepsy.

Study purposes are to determine as nearly as possible the incidence of the disease, the caseload among children, services available, services needed, educational services and attitudes, social implications, and estimated costs of full services should the condition be taken on as a fully eligible disease under Crippled Children Services.

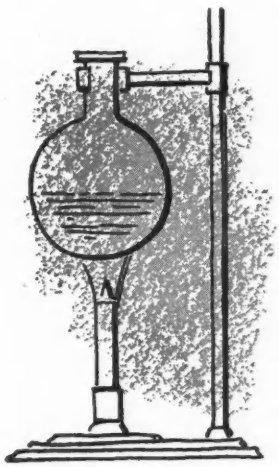
Dr. Harry E. Howard has joined the staff as medical officer in charge of the study. He left the position of district health officer with the San Francisco Health Department to take charge of the epilepsy project.

Standards for air quality and motor vehicle exhaust emissions were adopted by the State Board of Public Health in a December 4 meeting in Berkeley.

The standards were developed at the request of the Governor and the Legislature, and represent a pioneering effort in the field of air pollution control. They may very well establish a pattern for other states to follow.

* * *

The cost of certified copies of birth, death and marriage records will double January 1, from $1 to $2. The increase was enacted at the last session of the Legislature, and goes into effect in all local custodial offices and in the office of the State Registrar of Vital Statistics.



WOMAN'S AUXILIARY
TO THE CALIFORNIA MEDICAL ASSOCIATION

THE INITIALS WA/SAMA represent the Woman's Auxiliary to the Student American Medical Association. This auxiliary became a national organization in 1957 at Philadelphia.

Before that, the wives of medical students in several of the medical schools in this country were organized into social or study groups under such names as "Medwives" and "Medical Dames." In September 1955 the first chapter of the Woman's Auxiliary to the Student American Medical Association was developed at the University of Oklahoma School of Medicine.

The original idea for a student wives' organization is credited to Mrs. George H. Garrison of Oklahoma City. She wrote the following to the county auxiliaries in Oklahoma:

"Our auxiliary can scarcely afford to ignore so sincere a request for assistance. It will require very little outlay of effort or money on our part but the benefits that we will receive in future well-trained doctors' wives and the satisfaction that we have really served a need cannot be measured in hours and cents."

Wives of interns and residents in the area, as well as medical school students make up the Oklahoma group. They have described their purpose in organizing as twofold: to acquaint student wives with the profession of medicine and prepare them to take their position and responsibility as doctors' wives in the community where they may eventually settle; and to bring medical students and their wives into much-needed closer relationship with the local medical profession and their families for mutual benefit.

A one-year program outline suggested by these student wives covers a variety of topics. Included are a brief history of medicine, information about the medical school, a preview of the years to be spent there, the choices after medical schooling is completed, the doctor and his family, medical ethics, community responsibility, medical legislation and hobbies.

Panel discussions by doctors' wives on such matters as choice of location, finances and telephone etiquette and home-practice etiquette for wives are included in the program.

There are 38 chapters divided into eight geographical regions in 49 states, Puerto Rico and the District of Columbia. Chapter activities vary according to the needs and desires of local members. Membership in the auxiliary to the SAMA is open to the wife of any medical student, intern or resident. The aim of SAMA auxiliary is educational. What could be of more importance than learning to become good wives of men who deserve the best?

The student A.M.A. was formed in Chicago in 1950. Today the Association is composed of more than 55,000 active and affiliate members in 74 medical schools and hundreds of hospitals throughout the United States and its territories.

Constitutional provisions provide active membership to students in SAMA-affiliated schools without respect to race, religion, color or sex. Active members are medical students who join affiliated chapters and maintain both national and local dues structures; affiliate members are interns and residents; members-at-large are medical students in schools as yet unaffiliated or American students enrolled in foreign schools; honorary members are practicing physicians and friends of SAMA who maintain a continuing interest in the Association.

Except for the Executive Director and his staff, all officers, delegates and committee members are medical students, interns or residents. The constitution of the Association clearly defines the reason for its existence: "The objects of this Association shall be to advance the profession of medicine, to contribute to the welfare and education of medical students, interns and residents, to familiarize its members with the purposes and ideals of organized medicine, and to prepare its members to meet the social, moral and ethical obligations of the profession of medicine."

Thus we have the Student American Medical Association and auxiliaries joining the American Medical Association and its auxiliary "to assist the medical profession in its determined effort to provide the best medical care for the people of the world."

MRS. THEODORE A. POSKA
President, Woman's Auxiliary to the California Medical Association

INFORMATION

Tax Deductibility

The Status of Accident and Health Insurance Premiums

HOWARD HASSARD, San Francisco
Peart, Baraty & Hassard
General Counsel, California Medical Association

A RECENT decision of the Third Circuit Court of Appeals has again turned attention to the question of the deductibility of premiums paid for accident and health insurance. The Third Circuit ruled in the case of *Heard v. Commissioner*[1] that premiums paid for such insurance are deductible in their entirety as medical expenses even though they cover loss of life, limb, time and other disabilities. This ruling is contrary to the long established position of the Treasury that premiums for an accident and health policy insuring against loss of life, limb, sight and time are not medical expenses and thus nondeductible.

The purpose of this article is to analyze the effect of the Heard rule, and specifically its effect on the deductibility of premiums paid by members of the California Medical Association participating in the Association's group disability insurance plan.

Under the Association's group disability policy, which is titled "California Medical Association Disability Insurance Program," a subscribing member is insured against loss of life, limb, sight or time resulting from accidental bodily injuries, and for loss of time caused by sickness or disease. The Association also has a hospitalization policy under which participating members are reimbursed for hospital expenses. However, this latter insurance, termed "Catastrophic Hospitalization Insurance," is a separate contract with separate individual membership certificates issued thereunder and bears no relationship to the group disability policy. Premiums paid for hospitalization under the hospitalization insurance plan, are expenses paid for medical care and thus are fully deductible as medical expenses.

The Internal Revenue Service has taken the position in a series of rulings,[2] dating back to 1953, that premiums paid for accident and sickness benefit insurance that does not provide reimbursement to the insured for medical and hospital expenses are not deductible as a medical expense. In the event such a policy provides for both accident and sickness benefits *and* reimbursement for medical and hospital expenses, then only that portion of the premium attributable to the medical and hospital expenses is deductible as a medical expense. The decisions of the Tax Court are in accord[3] with that position. Thus, until the decision of the Third Circuit Court in the *Heard* case, it was well settled that disability insurance premiums were not deductible either as medical expenses or as business expenses.[4]

In the *Heard* case, the taxpayer paid premiums on policies providing benefits for accidental loss of life, limb, sight and time and also providing for reimbursement of medical expenses resulting from nondisabling accidents. The taxpayer deducted the total premium as a medical expense. The Tax Court held that only that part of the premium which provided for reimbursement of medical expenses qualified as a deductible medical expense. The Government officially acquiesced in the decision, announcing that the principle set by the ruling would be followed by the tax authorities. The case was then appealed to the Third Circuit Court of Appeals, which reversed the Tax Court, holding that the total premiums paid for health and accident policies were properly deductible as expenses for medical care, despite the fact that only a portion of each premium payment was attributable to medical or hospitalization coverage. The appellate court held that the tax law allows deduction of expenses paid for medical care, that the law includes "amounts paid for health or accident insurance" in the definition of medical care[5] and is not to be construed to exclude amounts paid to provide benefits for loss of life, limb, sight or time.

The Internal Revenue Service has issued a Revenue Ruling[6] stating that it will not follow the decision of the Third Circuit in the *Heard* case. The case is directly contrary to existing revenue rulings on the subject and has been criticized as running counter to established rules of statutory construction.[7] It must be pointed out that the decision is controlling law only in the geographical area covered by the Third Circuit Court of Appeals (Delaware, New Jersey, Pennsylvania and the Virgin Islands), and it is doubtful whether the case will be followed by the other circuit courts or by the tax courts. It is advisable for taxpayers in all other parts of the country to limit their deductions for premiums paid for accident and health insurance to those paid for medical expense coverage since in all probability any deduction for premiums expended for disability coverage will be disallowed by the Internal Revenue Service despite the *Heard* decision.

It can thus be seen that the *Heard* case for practical purposes will have little effect on the deduc-

tibility of premiums paid by California Medical Association members insured under the C.M.A. disability insurance policy. This insurance provides benefits only in event of the loss of life, limb, sight or time and contains no provision for reimbursement of medical or hospital expenses. The premiums paid for such insurance are thus not deductible as a medical expense under the rulings of the Internal Revenue Service that are still in full force and effect.

REFERENCES

1. 269 F. 2d 911.
2. Rev. Rul. 19, 1953—1 C. B. 59; Rev. Rul. 55-261, 1955—1 C. B. 307.
3. *D. C. Heard*, 30 T.C. 1093.
4. Rev. Rul. 55-331, 1955—1 C. B. 271.
5. Section 213 (e) Internal Revenue Code of 1954 (3).
6. Rev. Rul. 59-393, I.R.B. 1959-50, 52.
7. See discussion of this case in *Tax Barometer*, Vol. 16, Sec. 1652.

John Green's Rough Road To Smooth Sailing

The difficulties that beset Dr. John W. Green, of Vallejo, in getting home from the American Medical Association's December meeting in Dallas were a far cry from the serene life that so able a worker in the vineyard might reasonably expect upon retirement from years of service in the House of Delegates. However, not long afterward, a more suitable reward for the elder statesman was provided by his own townspeople. More later about the tribute of his neighbors, but first Dr. Green's own report of his memorable return from Dallas (taken from a letter he wrote to his long-time colleague, Dr. Donald Cass of Los Angeles):

December 7, 1959

Dear Don:

I had a bad time getting home from Dallas. You were very smart to go by rail. Our plane was grounded at Ontario due to fog, 60 miles by bus to Los Angeles International. I missed my connection with the United Air and took a coach to Burbank where I was a standby until 2:45 a.m. I arrived in San Francisco at 4:00 a.m. and got Ann [Mrs. Green] out of bed at my daughter's home. They waited for me until 2:30 a.m. and gave up.

Ann dressed and came down to the airport at 5:00 a.m. After a light breakfast we went to bed in Vallejo at 7:00 a.m. So ended my term of fourteen years in the "House."

Ann sends her regards.

Cordially,

PETE

P.S.—My luggage was lost in the shuffle but came by Greyhound Saturday afternoon.

And now, for a report of a more appropriate beginning for Dr. Green's contemplative years, we have a clipping from the *Vallejo Times-Herald:*

Dr. John W. Green, prominent Vallejo physician and surgeon who served as president of the California State Medical Association in 1953-54, was honored by the Vallejo Rotary Club yesterday for his contributions to organized medicine in California and the United States.

The guest speaker at the club's regular meeting in the Casa de Vallejo Hotel was Dr. Warren L. Bostick of San Rafael, a pathologist and councilor for the State Medical Association.

Doctor Bostick's subject was "John Green's California Medicine."

Also paying tribute to Doctor Green were Dr. H. B. Perkins and Dr. D. C. Marchand, both of Vallejo, who related anecdotes and incidents in the life of the Vallejo eye, ear, nose and throat specialist.

NEWS & NOTES

NATIONAL · STATE · COUNTY

FRESNO

Dr. Robb Smith, of Orange Cove, has been elected president of the **Central California Blood Bank** for 1960, succeeding Dr. John Murray of Fresno.

The bank serves 41 hospitals in Madera, Merced, Kings, Tulare and Fresno counties.

Other officers elected were Dr. J. J. McNearney, Tulare, vice president; Walter H. Stammer, Fresno, secretary, and Dr. Zdenek Fluss of Merced, treasurer.

LOS ANGELES

The 28th Annual Alumni **Postgraduate Convention of the College of Medical Evangelists** is scheduled for February 28 to March 3 in Los Angeles. The first two days of the five-day meeting will be at the College (Feb. 28, 29). The next three at the Ambassador Hotel (March 1-3) will feature six guest lecturers plus a prominent Los Angeles attorney and a number of faculty members from the University of Southern California, University of California at Los Angeles, and College of Medical Evangelists schools of medicine.

The first two days will consist of a series of refresher courses to be held in classrooms and laboratories on CME's Los Angeles campus. Physicians registered for these courses will receive Category I credit from the American Academy of General Practice.

* * *

Dr. Leo Rangell, a former president of the Southern California Psychiatric Society, was elected president-elect of the American Psychoanalytic Association at its recent annual meeting in New York City.

* * *

All members of the California Medical Association and their wives are invited to attend a **memorial mass** for our members who died during 1959, to be offered by His Eminence, J. Francis Cardinal McIntyre of Los Angeles. The mass will be held at St. Basil's Church, 658 South Harvard Boulevard at 8:00 a.m. on Monday, February 22. St. Basil's Church is located four blocks west of the Ambassador Hotel, on the corner of Wilshire and South Harvard Boulevards.

* * *

A number of ancillary organizations have scheduled meetings to be held in Los Angeles during the time of the Annual Session of the California Medical Association, as follows:

Southern California Chapter of the American Academy of Pediatrics, annual reception and dinner meeting, Wednesday, February 24, Ambassador Hotel, West Venetian Room. Reception at 6:30 p.m., dinner at 7:00 p.m. For information and reservations: Mrs. Jane Hausken, 600 D South Oak Knoll, Pasadena. Reservations, $6.50.

The California Academy of Preventive Medicine reception and dinner Tuesday, February 23, Ambassador Hotel, West Venetian Room, 6:30 p.m. For reservations and further information: G. A. Heidbreder, M.D., Secretary-Treasurer, California Academy of Preventive Medicine, 241 North Figueroa Street, Los Angeles 12.

California Chapter of the American College of Chest Physicians meeting and reception, Saturday, February 20, Embassy Room, meeting, 9:00 a.m. to 5:00 p.m.; reception, Regency Room, 5:00 to 7:00 p.m.

Conference of Local County Health Officers and County Society Representatives, Tuesday, February 23, West Venetian Room, 2:00 p.m.

* * *

There will be a meeting of the **Harvard Medical Alumni Association of Southern California** at the California Club, 538 South Flower, Los Angeles, at 6:30 p.m., Friday, March 11, to entertain Dr. Rolf Lium, president of Harvard Medical Alumni Association. Harvard medical alumni wishing to attend may obtain information from Dr. Lowell F. Bushnell, 1321 North Vermont Avenue, Los Angeles.

SAN FRANCISCO

A yearly **Low-Beer Lectureship in Radiation Therapy** has been established at the University of California Medical Center in honor of the late Dr. Bertram V. A. Low-Beer, professor of radiology until his death in 1955.

The purpose of this Lectureship is to bring distinguished visitors to the campus for a period of about one week, during which time the main address will be given.

The first Low-Beer Memorial Lecture will be held in the Auditorium, Medical Sciences Building, University of California Medical Center, San Francisco, on Thursday evening, March 3, at 8:00 p.m. Dr. Manuel Lederman, deputy-director of the Royal Marsden Hospital, London, will speak on "The Place of Radiation Therapy in the Treatment of Cancer of the Larynx."

GENERAL

Dr. John W. Cline, San Francisco, was elected chairman of the **Cancer Advisory Council** to the California State Department of Public Health at the organizational meeting of this recently appointed group. Dr. John Ross, Los Angeles, was elected vice chairman. The Council, made up of 15 members, nine of whom are physicians, was named in December by Governor Edmund Brown to advise in the enforcement of California's new anti-quackery law.

* * *

The American College of Surgeons will hold a section meeting in Portland, Oregon, March 28-March 30. The program will include scientific reports on topics of current concern such as five to ten-year results of radical masectomy for carcinoma, common ski injuries, treatment of hernia, injuries of the eyelids and globe, and duodenal ulcer.

* * *

The Eighth Congress of the **Pan-Pacific Surgical Association** will be held in Honolulu, Hawaii, September 27 through October 5 in 1960.

Further information and brochures may be obtained by writing to Dr. F. J. Pinkerton, director general of the Pan-Pacific Surgical Association, Suite 230, Alexander Young Building, Honolulu 13, Hawaii.

* * *

Dr. John Paul North, Dallas, Texas, will become the director of the **American College of Surgeons,** effective January 31, 1961, it was announced recently by Dr. I. S. Ravdin, chairman of the board of regents. He will succeed Dr. Paul R. Hawley, the College's Director.

POSTGRADUATE EDUCATION NOTICES

THIS BULLETIN of the dates of postgraduate education programs and the meetings of various medical organizations in California is supplied by the Committee on Postgraduate Activities of the California Medical Association. In order that they may be listed here, please send communications relating to your future medical or surgical programs to: Mrs. Margaret H. Griffith, Director, Postgraduate Activities, California Medical Association, 2975 Wilshire Boulevard, Los Angeles 5.

UNIVERSITY OF CALIFORNIA AT LOS ANGELES

CLINICAL POSTGRADUATE PROGRAM—MEXICO CITY, IN COOPERATION WITH THE NATIONAL SCHOOL OF MEDICINE, MEXICO CITY. Anesthesiology, Gastroenterology, Dermatology, Cardiology, Pediatrics and General Surgery. Feb. 25 through March 5, 1960.

Clinical Traineeships — Anesthesia, Dermatology and Pediatric Cardiology. Dates by arrangement. Minimum period—two weeks. Fee: Two weeks, $150.00; four weeks, $250.00.

Ophthalmic Plastic Surgery. Friday and Saturday, March 11 and 12. Twelve hours. Fee: $40.00 includes lunch.

Geriatrics in Clinical Practice. Saturday and Sunday, March 19 and 20. 12 hours. Fee: $40.00.

Emotional Problems in Pediatric Practice. Friday through Sunday, April 8 through 10. University of California Residential Conference Center, Lake Arrowhead. 13 hours. Fee: $110.00, including room and meals.

Inhalation Therapy. April.†

Postgraduate Medical Symposium. Grossmount Hospital, San Diego. Saturday and Sunday, April 30 and May 1. Twelve hours. Fee: $25.00.

Management of Medical Emergencies. Friday and Saturday, May 6 and 7. 12 hours.*

Low Back Pain. May.†

Proctology. Wednesday, June 8. Six hours.*

General Pediatrics. Sunday through Wednesday, July 17 through 20. Lake Arrowhead, University of California Residential Conference Center. Fifteen hours.*

Advance Seminar in Internal Medicine. Wednesday through Sunday, July 20 through 24. University of California Residential Conference Center, Lake Arrowhead. Eighteen hours.*

Dermatology in Office Practice. Monday and Tuesday, July 25 and 26. Twelve hours.*

Seminars in Dermatology (for Dermatologists). Wednesday through Saturday, July 27 through 30. University of California Residential Conference Center, Lake Arrowhead. Fifteen hours.*

Anesthesiology. Wednesday, Thursday and Friday, August 3, 4 and 5. Eighteen hours.*

Arthritis and Rheumatism. Wednesday, August 24.‡

The Multiple Injury Patient. Thursday, Friday and Saturday, September 22, 23, and 24. Eighteen hours.*

For Ancillary Personnel

Medical Terminology—Advanced. Tuesdays, February 16 through June 21. Forty-five hours. Fee: $35.00.

Beginning Medical Terminology. Wednesdays, February 17 through June 22. Forty-five hours. Fee: $35.00.

Pathological Physiology in Physical Treatment Procedures. Mondays, February 29 through April 25. Sixteen hours. Fee: $30.00.

Workshop in Practical Tuberculosis Bacteriology. Saturday, March 5. Eight hours. Fee: $5.00.

Contact: Thomas H. Sternberg, M.D., assistant dean for Postgraduate Medical Education, U.C.L.A., Los Angeles 24. BRadshaw 2-8911, Ext. 7114.

UNIVERSITY OF CALIFORNIA, SAN FRANCISCO

Psychotherapy in Medical Practice. Wednesdays, February 17 through May 4. Sixty hours. Fee: $25.00.

Course for Physicians in General Practice (Mt. Zion Hospital, San Francisco). Monday through Saturday, March 7 through 12. Thirty-eight hours. Fee: $85.00.

Patients As People—Evening Seminars on the Psychological Aspects of Medical Practice. Thursdays, March 10-May 26. Twenty-four hours. Fee: $5.00.

Diagnostic Radiology. Wednesday through Sunday, March 16 through 20. Thirty-five hours. Fee: $80.00.

Medical Evening Series (Eden Hospital, Castro Valley). Tuesdays, March 22 to May 10. Sixteen hours. Fee: $35.00.

Physiological Basis for Diagnosis and Treatment. An Official Course of the American Physiological Society. Wednesday through Sunday, March 30 through April 3. Thirty-five hours. Fee: $90.00 or $25.00 per day.

Symposium on Pediatric Surgery (Children's Hospital). Saturday, April 23. Seven hours. Fee: $12.50.

A Course on General Surgery. Monday to Friday, April 25 to 29. Thirty-five hours.*

A Course on Urology. Thursday and Friday, May 5 and 6. Fourteen hours.*

A Course on Ear, Nose, Throat. Thursday to Saturday, May 12 to 14. Twenty-one hours.*

Proctology. Thursday and Friday, May 19 and 20. Fourteen hours.*

Advances in Surgical Anatomy, Normal Anatomy and Histology of the Eye. Thursday to Saturday, June 2 to 4. Twenty-one hours.*

A Course on the Foot. Thursday to Saturday, June 9 to 11. Twenty-one hours.*

A Course in Industrial Medicine. Wednesday to Friday, June 22 to 24. Twenty-one hours.*

A Course on New Drugs. Thursday to Saturday, July 14 to 16. Twenty-one hours.*

Obstetrics and Gynecology. Thursday to Saturday, September 15 to 17. Twenty-one hours.*

Fundamental Practices of Radioactivity and the Diagnostic and Therapeutic Uses of Radioisotopes. Two or three month course limited to one enrollee per month. Fee: $350.00.

*Fees to be announced.
†Dates, fees and hours to be announced.
‡Hours and fees to be announced.

For Ancillary Personnel

Advances in Psychiatric Nursing: Section I.—All registered nurses. Wednesday, February 24 through April 13. Sixteen hours. Fee: $25.00.

Advances in Psychiatric Nursing: Section II.—Nurses who have had training and practice in Psychiatric Nursing. Thursdays, February 25 through April 14. Sixteen hours. Fee: $25.00.

Practical Cytology. Saturday and Sunday, February 27 and 28. Eleven hours. Fee: $15.00.

Rehabilitation Nursing. Monday through Friday, April 11 through 29. Fairmont Hospital, San Leandro.*

Evening Lectures on Pharmacy. Mondays, April 18 to May 23.*

Nursing Care of Mothers and Children. Tuesdays, April 19 through June 7, Highland Hospital, Oakland. Sixteen hours. Fee: $25.00.

Nursing Care of Medical-Surgical Patients. Thursdays, April 21 through June 9. Highland Hospital, Oakland. Sixteen hours. Fee: $25.00.

Nursing and People. Monday to Friday, May 2 to 13. Fee: $30.00.

Continuing Education Conference. Monday through Friday, June 13 through 17.*

Integration of Psychiatric Principles in the Total Curriculum. Tuesday to Friday, July 5 to August 12.*

Supervision. Tuesday through Friday, September 6 through 16.*

Administration of Nursing Care. Tuesdays, September 13 through December 13.*

Nutritional Aspects of Nursing Care. Wednesdays, September 21 through November 9.*

Contact: Seymour M. Farber, M.D., assistant dean, Department of Continuing Medical Education, University of California Medical Center, San Francisco 22. MOntrose 4-3600, Ext. 665.

STANFORD UNIVERSITY SCHOOL OF MEDICINE

Morning Clinical Conferences, each Monday. *Contact:* D. H. Pischel, M.D., Professor, Division of Ophthalmology, Stanford University School of Medicine, Stanford Hospital, Clay and Webster Streets, San Francisco.

For information contact: Dean, Stanford University School of Medicine, 300 Pasteur Drive, Palo Alto.

UNIVERSITY OF SOUTHERN CALIFORNIA, LOS ANGELES

Cardiac Resuscitation. Sponsored by the Los Angeles County Heart Association each Wednesday throughout the year, 4 to 6 p.m. USC Medical Research Building, Room 211, 2025 Zonal Avenue. Residents and interns of Los Angeles County, and all armed forces medical personnel admitted without fee. Tuition for all other physicians: $30.00. (Each session all-inclusive.)

Basic Home Course in Electrocardiography. One year postgraduate series, electrocardiogram interpretation by mail. Physicians may register at any time and receive all 52 issues. Fifty-two weeks. Fee: $100.00.

*Fees to be announced.

Advance Home Course in Electrocardiography. One year postgraduate series, electrocardiogram interpretation by mail. Fifty-two issues: $85.00. Physicians may register at any time.

Dermatology Clinic, One-Day Symposium. Thursday, March 24. Seven hours. Fee: $25.00.

Symposium on Hypertension. Friday, April 1. Seven hours. Fee: $7.50.

Funduscopy in Internal Medicine. Every other Tuesday, April 5 through June 14. Twelve hours. Fee: $37.50.

Ward Walks in Rare Diseases. Thursdays, April 14 through June 16. Twenty hours. Fee: $100.00.

Practical Diagnosis and Management of Cardiovascular Diseases. Dates to be announced. Twenty-one hours. Fee: $75.00.

Contact: Phil R. Manning, M.D., associate dean and director, Postgraduate Division, University of Southern California School of Medicine, 2025 Zonal Avenue, Los Angeles 33. CApital 5-1511.

COLLEGE OF MEDICAL EVANGELISTS

CLINICAL TRAINEESHIPS available in all clinical departments by arrangement with the Postgraduate Division and the chairman of the department or departments involved. Eighty hours minimum. Fee: As arranged.

Diseases of the Chest: Two and four-week Traineeships in cooperation with the Los Angeles County Hospital. Dates as arranged.

Anesthesia. Monday through Friday. Dates as arranged. Six months. Fee: $350.

SPECIAL SKILLS available in the clinical departments, usually with a maximum of two or three students.

Surgical Anatomy: Head and Neck, April 20 through June 1, 63 hours. Fee: $75.00.

Surgical Anatomy: Head and Neck, April 20 through June 1. Twenty-four hours. Fee: $35.00.

ALUMNI POSTGRADUATE CONVENTION, held annually in cooperation with the Alumni Association of the School of Medicine. Refresher Courses, Sunday and Monday, February 28 and 29, at White Memorial Hospital, 1720 Brooklyn Avenue. Six hours each day. Fee: $20.00 each day. Scientific Assembly, Tuesday through Thursday, March 1 through 3, at the Ambassador Hotel. Twenty-four hours. Fee: $15.00. *Contact:* Walter Crawford, executive secretary, 316 N. Bailey Street, Los Angeles 33, ANgelus 2-2173.

TRAUMATOLOGY, a complete review including fractures and dislocations, soft tissue injuries, as well as complications involving the 3 cavities: Calvarium, thorax and abdomen. Limited to 15 candidates. Includes basic sciences, lectures, clinical demonstrations. Monday through Friday, March 7 through 11. Thirty-six hours. Fee: $100.00.

TROPICAL PUBLIC HEALTH: Causes, treatment and management of diseases found in the warm climates. For physicians who plan to serve abroad and other ancillary personnel. Monday through Friday, April 1 through May 30. Fee: $65.

JOINT MANIPULATION. Monday through Friday, 8:00 to 12:00, dates to be arranged. Twenty hours. Fee: $75.00.

For information contact: G. E. Norwood, M.D., assistant dean and chairman, Division of Postgraduate Medicine, College of Medical Evangelists, 1720 Brooklyn Ave., Los Angeles 33. ANgelus 9-7241, Ext. 214.

CALIFORNIA MEDICAL ASSOCIATION POSTGRADUATE COURSES

ANNUAL SESSION POSTGRADUATE COURSES

Infectious Diseases. 9 hours. Sunday, Monday and Tuesday, February 21, 22 and 23, 9:00 to 12:00 noon. February 21 at Chapman Park Hotel, February 22 and 23 at Ambassador Hotel, Los Angeles. Program by University of California School of Medicine, Los Angeles.

Clinical Endocrinology. 9 hours. Sunday, Monday and Tuesday, February 21, 22 and 23, 9 to 12 noon. February 21 at Los Angeles County Hospital, February 22 and 23 at Ambassador Hotel. Program by University of Southern California School of Medicine.

Minor Surgery. 9 hours. Sunday, Monday and Tuesday, February 21, 22 and 23, 9 to 12 noon. All sessions at White Memorial Hospital, Los Angeles. Program by College of Medical Evangelists.

POSTGRADUATE INSTITUTES—1960
(Tenth Anniversary Year)

North Coast Counties in cooperation with College of Medical Evangelists, March 31 and April 1. Flamingo Hotel, Santa Rosa. *Chairman:* H. Ward Wick, M.D., 858 Fourth Street, Santa Rosa.

Southern Counties in cooperation with Stanford University School of Medicine, April 21 and 22. Palm Springs Riviera. *Chairman:* Robert M. Zweig, M.D., 7004 Magnolia, Riverside.

San Joaquin Valley Counties in cooperation with University of Southern California School of Medicine, April 28 and 29. Ahwahnee Hotel, Yosemite. *Chairman:* Campbell H. Covington, M.D., 2057 High Street, Selma.

Sacramento Valley Counties in cooperation with UCLA School of Medicine, July 1 and 2. Tahoe Tavern, Lake Tahoe. *Chairman:* Herbert W. Korngold, M.D., 1217 30th Street, Sacramento.

Contact: One of the chairmen listed above, or Postgraduate Activities Office, California Medical Association, 2975 Wilshire Boulevard, Los Angeles 5.

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AUDIO-DIGEST FOUNDATION, a nonprofit subsidiary of the C.M.A., offers (on a subscription basis) a series of six different hour-long tape recordings covering general practice, surgery, internal medicine, obstetrics and gynecology, pediatrics and anesthesiology. Designed to keep physicians posted on what is new and important in their respective fields, these programs survey current national and international literature of interest and contain selected highlights of on-the-spot recordings of national scientific meetings, panel discussions, symposia, and individual lectures. For information contact Mr. Claron L. Oakley, Editor, 1919 Wilshire Blvd., Los Angeles 57, HUbbard 3-3451.

Medical Dates Bulletin

FEBRUARY MEETINGS

CALIFORNIA MEDICAL ASSOCIATION Annual Meeting, February 21 through 24, Ambassador Hotel, Los Angeles. *Contact:* John Hunton, executive secretary, 693 Sutter Street, San Francisco 2; or Ed Clancy, director of Public Relations, 2975 Wilshire Blvd., Los Angeles 5.

PACIFIC COAST SURGICAL ASSOCIATION Annual Meeting. February 21 through 24. Palm Springs. *Contact:* Carleton Mathewson, M.D., professor of surgery, Stanford Hospital, San Francisco.

MARCH MEETINGS

SOUTHWESTERN PEDIATRIC SOCIETY Spring Lecture Series, March 1 and 2, Statler Hotel, Los Angeles. *Contact:* Wendell Severy, M.D., program chairman, 11633 San Vicente Blvd., Los Angeles 49.

ANESTHESIA SECTION, LOS ANGELES COUNTY MEDICAL ASSOCIATION, Fifth Annual Course in Anesthesiology for Physicians. March 12 and 13. 1925 Wilshire Blvd., Los Angeles. *Contact:* Thomas W. McIntosh, M.D., chairman, 686 East Union St., Pasadena.

PIONEERS MEMORIAL HOSPITAL MEDICAL STAFF in association with the University of Oklahoma School of Medicine, Tenth Annual Postgraduate Assembly. March 18 and 19. Pioneers Memorial Hospital, Brawley. *Contact:* George C. Holleran, M.D., program chairman, P. O. Box 159, Brawley, Calif.

SAINT JOSEPH HOSPITAL, BURBANK, Annual Medical Assembly. March 25 and 26, 9 to 5 p.m. Saint Joseph Hospital Auditorium, 501 S. Buena Vista, Burbank. *Contact:* Walter Gelb, Public Relations, St. Joseph Hospital, 501 S. Buena Vista, Burbank, THornwall 8-5531, Ext. 305.

AMERICAN SOCIETY OF MAXILLOFACIAL SURGEONS, Ambassador Hotel, Los Angeles. March 27 through 31. *Contact:* Arthur E. Smith, M.D., D.D.S., 1930 Wilshire Blvd., Los Angeles 57.

INTERMOUNTAIN PEDIATRIC SOCIETY, Stardust Hotel, Las Vegas, Nevada. March 28 and 29. *Contact:* Joseph R. Newton, M.D., publicity chairman, 2000 S. 9th East, Salt Lake City, Utah.

SOUTHWESTERN SURGICAL CONGRESS. March 28 through 31, Riviera Hotel, Las Vegas, Nevada. *Contact:* Miss Mary O'Leary, executive secretary, 1213 Medical Arts Building, Oklahoma City, Oklahoma.

NEUROSURGICAL SOCIETY OF AMERICA. March 30 through April 2, Del Monte Lodge, Del Monte. *Contact:* Raymond K. Thompson, M.D., secretary, 803 Cathedral Street, Baltimore 1.

APRIL MEETINGS

AMERICAN SOCIETY OF INTERNAL MEDICINE. April 1 through 3. Palace Hotel, San Francisco. *Contact:* Mr. Robert L. Richards, executive director, 350 Post Street, San Francisco 8.

AMERICAN COLLEGE OF PHYSICIANS Annual Meeting, April 4 through 9. Civic Auditorium, San Francisco. *Contact:* Edward C. Rosenow, Jr., M.D., executive director, 4200 Pine Street, Philadelphia 4.

HARVEY CUSHING SOCIETY. Fairmont Hotel, San Francisco. April 13 through 17. *Contact:* Edmund J. Morrissey, M.D., 450 Sutter Street, San Francisco 8.

CALIFORNIA MEDICAL ASSISTANTS ASSOCIATION Annual Convention. April 23 and 24. Claremont Hotel, Berkeley. *Contact:* Mrs. Anne Reece, president CMAA, 1837 So. Indiana St., Porterville, California.

VALLEY CHILDREN'S HOSPITAL Spring Clinics. April 28 through 30. Roosevelt High School auditorium, Fresno. *Contact:* Valley Children's Hospital, Shields and Millbrook Avenues, Fresno.

MAY MEETINGS

PAN AMERICAN MEDICAL ASSOCIATION CONGRESS. May 2 to 11. Mexico City. *Contact:* Joseph J. Eller, M.D., director general, 745 Fifth Avenue, New York, N. Y.

MEMORIAL HOSPITAL OF LONG BEACH Medical Staff 2nd Annual Scientific Symposium "New Horizons in Medicine," to be held in conjunction with the formal opening of the new 400-bed Memorial Hospital of Long Beach. May 4. *Contact:* George X. Trimble, M.D., director of medical education, Seaside Memorial Hospital, 1401 Chestnut Avenue, Long Beach 13.

STUDENT AMERICAN MEDICAL ASSOCIATION, Statler-Hilton Hotel, Los Angeles, May 5 through 8. *Contact:* Mr. R. F. Staudacher, executive director, 430 N. Michigan, Chicago 11.

NEVADA ACADEMY OF GENERAL PRACTICE 1960 Annual Assembly. May 12 through 14. Riverside Hotel, Reno, Nevada. Scientific program by University of California School of Medicine. *Contact:* Roy M. Peters, M.D., general chairman, 475 So. Arlington, Reno, Nevada.

HAWAII MEDICAL ASSOCIATION Annual Meeting. May 12 through 15. *Contact:* Miss Lee McCaslin, executive secretary, 510 S. Beretania, Honolulu 13.

NATIONAL TUBERCULOSIS ASSOCIATION—AMERICAN TRUDEAU SOCIETY Annual Meeting. May 16 through 19. Statler Hilton and Biltmore Hotels, Los Angeles. *Contact:* Mr. Sherman Asche, general chairman, Annual Meeting Committee, P. O. Box 4037, Santa Barbara.

AMERICAN COLLEGE OF NUTRITION 1960 Annual Convention. May 20 through 22. Huntington Sheraton Hotel, Pasadena. *Contact:* Donald B. Haynie, executive secretary, 10651 West Pico Blvd., Los Angeles 64.

CALIFORNIA HEART ASSOCIATION Annual Meeting and Scientific Session. May 23 through 25. Claremont Hotel, Berkeley. *Contact:* J. Keith Thwaites, executive director, 1428 Bush Street, San Francisco 9.

SUMMER AND FALL 1960 MEETINGS

GERONTOLOGICAL SOCIETY, INC., Mark Hopkins Hotel, San Francisco. August 7 through 12. *Contact:* Mrs. Marjorie Adler, administrative secretary, 660 S. Kingshighway Blvd., St. Louis 10.

RENO SURGICAL SOCIETY 10th Annual Conference. August 18, 19 and 20. The Mapes Hotel, Reno. *Contact:* Harry B. Gilbert, M.D., 275 Hill Street, Reno, Nevada.

AMERICAN ASSOCIATION OF BLOOD BANKS, Jack Tar Hotel, San Francisco. August 21 through 26. *Contact:* John B. Alsever, M.D., secretary, 1211 W. Washington St., Phoenix, Arizona.

AMERICAN HOSPITAL ASSOCIATION, Civic Auditorium, San Francisco. August 27 through September 1. *Contact:* Mr. Maurice J. Norby, assistant director, 18 E. Division St., Chicago.

NEVADA STATE MEDICAL ASSOCIATION Annual Meeting. September 7 through 10. Stardust Hotel, Las Vegas. *Contact:* Nelson B. Neff, executive secretary, P. O. Box 2790, Reno, Nevada.

CALIFORNIA SOCIETY OF INTERNAL MEDICINE Annual Meeting, Yosemite. September 23, 24 and 25. *Contact:* Barbara E. Oulton, executive secretary, 350 Post St., San Francisco 8.

PAN-PACIFIC SURGICAL ASSOCIATION 8th Intensive Surgical Congress, embracing all Surgical Specialties. September 28 through October 5. Honolulu, Hawaii. *Contact:* F. J. Pinkerton, M.D., director general, Suite 230, Alexander Young Building, Honolulu 13.

AMERICAN ASSOCIATION FOR THE SURGERY OF TRAUMA. Coronado Hotel, San Diego. October 5 through 7. *Contact:* William T. Fitts, Jr., M.D., secretary, 3400 Spruce St., Philadelphia 4.

WESTERN INDUSTRIAL MEDICAL ASSOCIATION combined Meeting with 4th Western Industrial Health Conference. October 7 through 9. Jack Tar Hotel, San Francisco. *Contact:* Verne G. Ghormley, M.D., president, 3032 Tulare Street, Fresno 21.

AMERICAN COLLEGE OF SURGEONS, Clinical Congress, San Francisco. October 10 to 14. *Contact:* H. P. Saunders, M.D., 40 E. Erie St., Chicago 11.

AMERICAN SCHOOL HEALTH ASSOCIATION, San Francisco. October 30 through November 4. *Contact:* A. O. DeWeese, M.D., executive secretary, 515 E. Main St., Kent, Ohio.

AMERICAN PUBLIC HEALTH ASSOCIATION, San Francisco. October 31 through November 4. *Contact:* Berwyn F. Mattison, M.D., executive director, 1790 Broadway, New York 19.

THE PHYSICIAN'S *Bookshelf*

DIFFERENTIAL DIAGNOSIS OF ABDOMINAL PAIN, THE—University of California Medical Extension Series, Los Angeles—Edited by Sherman M. Mellinkoff, M.D., Associate Professor of Medicine, UCLA School of Medicine, Los Angeles. The Blakiston Division, McGraw-Hill Book Company, Inc., New York, 1959. 443 pages, $9.00.

Two internists, a surgeon and a urologist have joined forces to compose an excellent postgraduate symposium on abdominal pain for the practitioner. Thorough reading of this small volume can substitute for the postgraduate course that the practitioner might have taken at the University of California School of Medicine at Los Angeles. And by using it he may polish up on his medical school habits and jargon as well as on his diagnostic ability.

This volume catalogs systematically and briefly the known causes of abdominal pain and describes or makes available by reference the means by which these can be recognized and differentiated. The rather novel approach of having two internists combine with a surgeon and urologist to present such a text is designed to avoid overemphasis on too frequent surgery as well as to emphasize surgical treatment when it is indicated.

This is a good postgraduate symposium and we recommend it to practicing physicians.

EDGAR WAYBURN, M.D.

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PERIPHERAL VASCULAR DISEASES: AN OBJECTIVE APPROACH — Travis Winsor, M.D., F.A.C.P.: Assistant Clinical Professor of Medicine, University of Southern California School of Medicine, Los Angeles; Director, Heart Research Foundation, Los Angeles; Staff Member, The Hospital of the Good Samaritan, Los Angeles; Staff Member, St. Vincent's Hospital, Los Angeles; Staff Member, Los Angeles County General Hospital. With a foreword by Burrell O. Raulston, M.D., Dean Emeritus, University of Southern California, School of Medicine, Los Angeles, California. Charles C. Thomas, Publisher, 301-327 East Lawrence Avenue, Springfield, Illinois, 1959. 845 pages, $16.50.

A gradual evolution of the electrocardiograph during the early decades of the twentieth century has brought to clinical cardiology an exacting tool for measurements of cardiac function. Similarly, in the last twenty years, the electronic devices of the physiology laboratory have been perfected and have been made practical for the measurement of vascular and sympathetic nerve function, as related to clinical angiology. Doctor Winsor has long been a leader in these technicological areas, as well as in the field of vascular disease.

In his book, Peripheral Vascular Diseases, Winsor presents through these improved instruments an objective approach to the understanding and treatment of patients with peripheral vascular disease. There is adequate background coverage of the anatomy, physiology and dynamics of circulation. There is an accurate description of the physiologic tools with which Doctor Winsor is so familiar. These include physiologic transducers, segmental and digital plethysmography, rheoplethysmography, skin thermometry, capillary and scleral microscopy, oscillometry, ergography, vibrometry, as well as physical examination, arteriography and phlebography.

Drug therapy has been brought up to date and objective studies of the relation of the modern drug to results in various diseases are carefully considered, including anticoagulants and vasodilators. The use of physical methods of therapy, such as postural exercises, oscillating beds and cradles, are well presented. Doctor Winsor presents a careful and well thought out classification of peripheral vascular disease and then proceeds to consider each of the classes in a systematic, clear, brief manner. The illustrations are profuse and simple. In each case the illustrator has brought together the illustration as a summation of the printed matter, so that one can easily recall the detailed subject matter. It is as if one were in an exhibition booth with a constantly changing exhibit. This is a book which should be of value, not only to the general practitioner and the internist, but also to the researcher who may find herein tools for clinical investigation.

* * * R. S. GILFILLAN, M.D.

A GUIDE TO ANTIBIOTIC THERAPY—Henry Welch, Ph.D. Medical Encyclopedia, Inc., 30 East 60th Street, New York 22, N. Y., 1959. 69 pages, $3.00.

The purpose of this book is rather obscure. According to the introductory statement "an attempt has been made to condense for the physician's ready reference the important information concerning each of 31 antibiotics." Yet the book consists of a series of tables which list, for each drug, the susceptibility, *in vitro*, of large numbers of micro-organisms, without reference to the potential usefulness of the drug. Thus two half pages of yellow-white striped printing, listing some 50 names of micro-organisms, are dedicated to vancomycin, although this drug should never be considered in anything but staphylococcal infections. This might simply indicate a ludicrous waste of paper and printing, but it actually obscures, rather than clarifies information for the physician. In addition there is evident a complete lack of discrimination. Carbomycin is described on half a page for various hypothetical uses, although this drug has been virtually withdrawn from the market some years ago because it was the single poorest member of the erythromycin group of drugs, widely known as the "drug in desperate search for a disease." Yet no mention is made that this drug belongs to the erythromycin group.

Chlortetracycline (aureomycin) capsules are described on a whole page, without a single statement that this drug is a low-ranking member of the tetracycline group and should probably be used very rarely, if ever. The book also contains many factual errors: e.g., the average dose for adults of chloramphenicol capsules is stated to be 4 grams daily!

In the opinion of this reviewer most physicians would do well to avoid contact with this publication.

NAVY SURGEON—Rear Admiral Herbert Lamont Pugh (MC, Ret.). J. B. Lippincott Company, Philadelphia, 1959. 459 pages, $5.00.

The autobiography of Rear Admiral Herbert Lamont Pugh (MC, Ret.) is a rather extensive tome entitled Navy Surgeon. To the average reader, a less faithful recording of the extraneous details of his personal diary would have strengthened the book. However, to all young men contemplating a career in one of the services, it is recommended reading. The story is a faithful and inspiring account of how a young doctor of humble background reached the high office of Surgeon General of the United States Navy and, in so doing, achieved one of the most rewarding and fascinating of life's experiences.

The progenitors of the large Pugh family were God-fearing people of strong character. Attitudes of industry and thrift were as much a part of choice as necessity. From the father was learned the nobility of work and from the mother a reverence for God and the family. Young Lamont's years of training were often periods of hardship and self-sacrifice. The story reflects, however, a sense of dedication and appreciation of opportunity, with which he passed in succession the many milestones of his professional career.

It was the second world war which provided the opportunity for unprecedented advancement. One after the other of top assignments was given to Doctor Pugh. From the position of Chief of the Surgical Service at the Naval Hospital, Pearl Harbor, he was transferred in eight short months to the same position at the Naval Hospital, San Diego. Being the only member of the regular Navy at the time who had been certified through examination by the American Board of Surgery, Commander Pugh found himself in charge of a service having several members of his staff of senior rank. At one time Commander Pugh was the only member of the regular Navy on the San Diego staff of 185 surgeons, or specialists allied to surgery. His consistent habit of always qualifying himself for advancement through examination or elective training, had indeed paid rich dividends.

Both as Deputy Surgeon General and as Surgeon General, Doctor Pugh served a period of eight years in the Bureau of Medicine and Surgery. During that time many creative ideas for advancing the status and prestige of medicine as practiced in the armed services, were put into effect. It is today a fact that in the armed services medical program there are equality of training opportunity and many compensatory advantages to those who choose to serve their country in this way. Lamont Pugh's career is a living testimonial to the rewards which can accrue from this choice.

W. L. Rogers, M.D.
Rear Admiral, MC, USNR

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DIAGNOSIS AND TREATMENT OF MENSTRUAL DISORDERS AND STERILITY—Fourth Edition—S. Leon Israel, M.D., Professor of Gynecology and Obstetrics, Graduate School of Medicine, University of Pennsylvania; Chief Gynecologist, Graduate Hospital; Gynecologist and Obstetrician, Pennsylvania Hospital, Philadelphia. Paul B. Hoeber, Inc., Medical Book Department of Harper & Brothers, 1959. 666 pages, $15.00.

The fourth edition of this successful book appears as the sole effort of the former junior author with the exception of three sections written by collaborators. It is a relatively large volume since it is composed of 31 chapters and covers 666 pages.

Any writer on the subject of menstrual disorders is faced with the problem of how far afield he should go with the discussion of allied subjects such as endocrinology, gynecologic and systemic disease, and infertility. Israel seems to have faced this difficulty by including all of them. The book begins with a consideration of the physiology of the pituitary gland and the ovaries, and turns to a clinical evaluation of puberty, following which we find a description of the normal menstrual cycle, and a chapter is then interposed on the role of androgen in gynecic physiology. The various menstrual disorders are then taken in sequence, but amenorrhea is given special consideration and extensive sections are devoted to its appearance in derangements of the central nervous system, the pituitary gland, the ovaries, and the uterus. The role of the thyroid gland and adrenal cortex in menstrual disorders now receive special attention, and the next four chapters take up the problems of menorrhagia and metrorrhagia. Finally, seven chapters deal with various aspects of sterility, including the male factor, and the concluding section is devoted to recurrent abortion.

The assortment of so many topics and the arrangement adopted by the author at once lead one to suspect that we may be faced with a confused mass of material. There is indeed some irregularity in the assessment of the relative values of some subjects. For instance, in a book on menstrual disorders one would expect more than nine pages of text dealing with the menopause, especially since neoplastic disease is given fifteen pages and includes a discussion of carcinoma in situ of the cervix which has nothing to do with derangements of menstruation and is not even characterized by abnormal bleeding. However, a careful perusal of the book shows that this divergence does not detract from it but in many ways enhances its value. The reason is that it is remarkably well done. Each disorder or disease is given a concise clear description, the diagnostic procedures are well defined, and treatment is presented in a definite usable manner. The author does not have any ax to grind and his approach to the endocrine therapy of menstrual disorders is conservative and sound, while he avoids the regrettable abuses which have characterized this subject since the early days of the ovarian residue pills. Israel is an accomplished writer and the book reads well; we may forgive him for the occasional lapse such as "the midinternally administered estrogen" and "the ferning of the cervical mucus."

This is an excellent and authoritative book, far more complete than its predecessors, and it is certain to appeal to a wider group of practitioners than merely to the specialties implied in the title.

C. Frederic Fluhmann, M.D.

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INTERN'S MANUAL (Cook County Hospital)—Second Edition—Arthur Bernstein, M.D., Assistant Medical Superintendent, Cook County Hospital; Clinical Associate Professor of Medicine, University of Illinois College of Medicine. The Year Book Publishers, Inc., 200 East Illinois Street, Chicago 11, 1959. 308 pages, $3.00.

This little volume essentially outlines methods of diagnosis and treatment of major illnesses as they are cared for at the Cook County Hospital. As the name indicates, the volume is primarily designed for interns at the Institution. The book outlines in a concise way a satisfactory management of most of the major illnesses. In a sense it contains the orders that the interns are to write in particular conditions.

While the book undoubtedly would be most valuable to an intern at the Cook County Hospital, interns at other institutions will also find it valuable, particularly in the early portion of the intern year. The book could also serve as a check list for a practicing physician who might utilize it to be sure that he had not omitted certain aspects of therapy. This sort of volume could be dangerous in that it could give either intern or practicing physician a "cook book" approach to therapy. Nevertheless, as the author plans its use, the book should prove valuable.

GROUP PSYCHOTHERAPY — Theory and Practice — Second Edition—J. W. Klapman, M.D., Consultant, Downey Veterans Hospital, Diplomate Board of Psychiatry and Neurology. Formerly Faculty, Northwestern University Medical School. Grune & Stratton, 381 Fourth Avenue, New York 16, N.Y., 1959. 301 pages, $6.75.

The second of Klapman's *Group Psychotherapy* (the first edition appeared in 1946) is a difficult one to evaluate. This is because, while it presents much that is of practical value and does reveal a sensitivity to the therapeutic needs of patients, the theoretical basis of the book is a confusing hodge-podge ecclecticism. It contains elements of Learning Theory, Kurt Lewin's Field Theory, and Adlerian Ego Psychology, along with halfhearted acceptance of Psychoanalytic Theory.

The author grants the importance of psychoanalytic concepts of transference and resistance and then proceeds to redefine these concepts. An author certainly has a right to accept or reject any concept. However, to state that he accepts a concept, such as transference, and then to proceed to redefine it in such a way as to distort an already established meaning, only serves to confuse the newcomer in the field and to add semantic difficulties to existing problems. The concept of resistance also is so loosely used as to include any expressions of feeling which are not "positive"—as, for example, sibling rivalry in a group is referred to as an expression of "resistance." Frequently Freud is quoted out of context in a manner calculated to denigrate the importance of drives and defenses in group therapy.

The author points up the usefulness of group therapy in clarifying, and correcting distorted patterns of ego functioning, especially as they apply to interpersonal relationships. However, the "ego" the author refers to is conceptualized in terms of Adler, Horney, and Eric Fromm. The role of intrapsychic forces on ego functioning is minimized to the point where the author states that "affects may be the servant of perception rather than the other way around." To discuss ego psychology in 1959 without mentioning anywhere the contributions of Hartmann, Eric Ericson, and Rappaport is a serious shortcoming in a book dealing with current concepts of ego functioning, as they apply to group therapy.

Despite these weaknesses in theoretical orientation the book has value from a pragmatic viewpoint. The division of the book into chapters describing handling of patients with minimal, moderate, and finally with severe states of personality disorganization is a useful approach. The glaring distortions of more commonly accepted concepts of intrapsychic functioning are less apparent in discussions of treatment of moderately and severely disturbed individuals. This is because in such individuals one must focus on ego reintegration, and a suppressive, reeducative type of therapy, rather than an uncovering type, is indicated.

The ideas presented in regard to many technical procedures are discussed in a manner which would stir little controversy among experienced group therapists, and would be of value to the neophyte. These include the choice of patients for various types of groups, suggestions regarding indications and contra-indications, and some discussion regarding typical problems arising in group therapy, such as handling of initial hours, silences, post therapy hour get-together of patients, etc.

It may be of value to compare this book with another recent text on group therapy by Corsini. This author sharply delineates the differences between an analytically oriented approach to group therapy from other approaches, such as a Rogerian "client centered non-directive" approach utilizing actual transcriptions of therapy hours to demonstrate the differences and similarities. Corsini avoids judgments as to the superiority of one technique over the other, but the reader is able to get a clear concept of the various approaches without distortion.

For anyone seriously interested in learning what group therapy has to offer, Klapman's book would be of much greater value after one has first read a text such as Corsini's. Klapman's book does have a good index and a fairly comprehensive bibliography which enhance the value of the book.

MICHAEL ROSOW, M.D.

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DISTURBANCES IN GASTROINTESTINAL MOTILITY—Edited by J. Alfred Rider, M.D., Ph.D., Assistant Professor of Medicine, University of California School of Medicine, San Francisco, California; and Hugo C. Moeller, M.D., Ph.D., Assistant Professor of Medicine, University of California School of Medicine, San Francisco, California. Charles C. Thomas, Publisher, Springfield, Illinois, 1959. 387 pages, $13.00.

This book is the recording of a symposium oriented around the central theme of gastrointestinal motility. A large number of distinguished authors have contributed sections on subjects ranging from the basic physiology of swallowing to the therapy of ulcerative colitis. Some of the clinically important topics covered include the following: The treatment of constipation and diarrhea, gall bladder and biliary tract disease, malabsorption syndromes, infectious diarrhea, diarrhea in the young child, regional enteritis and postgastrectomy syndromes. There are transcripts of stimulating conferences on ulcerative colitis and functional constipation. The book summarizes a great deal of newly acquired information about basic aspects of gastrointestinal physiology and also much wisdom on certain practical aspects of therapy. In the opinion of the reviewer a few of the views expressed on certain controversial subjects, such as biliary dyskinesia (by J. Dudfield Rose) would not be universally accepted. Nevertheless, no one interested in a stimulating reappraisal of this broad subject could fail to enjoy reading this book and important data and references would be made available by having this volume in one's own library.

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A WAY OF LIFE AND SELECTED WRITINGS OF SIR WILLIAM OSLER—An Unabridged and Unaltered Republication of 1951 edition "Selected Writings of Sir William Osler" (Oxford University Press). Paperback edition published by permission of Oxford University Press by Dover Publications, Inc., 180 Varick Street, New York 14, N. Y. 278 pages, paperback, $1.50.

Now that few remain who knew Osler personally there has been a lively revival of interest in his general and historical writings. This takes the form of reprints of Osler's essays, volumes which include selections from his various writings, and even anthologies of quotations. It is interesting to see a reprint of selected writings of Sir William Osler, first collected in 1951, now reprinted by the Dover Publications in an inexpensive but pleasant format which makes possible a wide circulation among medical students and those who cannot afford expensive books.

The collection contains a wide sampling of Sir William's writings: historical essays, talks to students, bibliophilic material and so forth. On looking through the book one finds that these brilliant essays—coruscating with literary allusions—can not only be reread but their pertinence in this mechanistic age becomes even more impressive. Osler, it now seems clear—will occupy a permanent place in English belles lettres.

ARTHUR L. BLOOMFIELD, M.D.